ine the total paralysis situation in darkness as well as in well-illuminated visual fields in order to decide on the source of EEPI.

LEONARD MATIN
EVAN PICOULT
Department of Psychology, Columbia University, New York 10027
JOHN K. STEVENS
Department of Physiology and *Playfair Neuroscience Unit, University of Toronto, Toronto, Ontario, Canada M5T 2S8*
MCIVER W. EDWARDS, JR.
Department of Anesthesiology, University of Pennsylvania, Philadelphia 19104
DAVID YOUNG*
RODGER MACARTHUR†
Department of Psychology, Columbia University

References and Notes

1. Extraretinal eye position information (EEPI) refers to any information which the observer has about the orientation of his eye in the orbit that does not arise from visual stimulation of the retina by light. EEPI has been considered to originate in (i) neural centers generating the command to turn the eyes (outflow theory), (ii) sense organs in extraocular musculature or retrobulbar tissue (inflow theory), or (iii) sense organs in extraocular musculature where the afferent signals are modulated by efferent signals or from other more central regions generating feedback regarding the efficacy of the command (hybrid theory) [for reviews, see L. Matin, in *Handbook of Sensory Physiology*, vol 7, part 4, *Visual Psychophysics*, D. Jameson and L. M. Hurvich, Eds. (Springer-Verlag, Heidelberg, 1972), pp. 331–380; *Perception* **5**, 233 (1976); in *Tutorials on Motion Perception*, A. Wertheim, W. A. Wagenaar, H. W. Leibowitz, Eds. (Plenum, New York, in press)].
2. A total of ten sessions was run on the five subjects: four on L.M., two each on J.S. and D.Y., and one each on E.P. and R.M. *d*-Tubocurarine was given in doses of 0.05 mg/kg every 5 minutes until the desired level of paralysis was achieved and then continuously infused at a rate of about 9 mg/hour for a total of 20 to 30 mg during the 2- to 4-hour session. At the level of paralysis used during quantitative psychophysical work speech was barely audible, the arm could barely be raised from the lap, expiratory vital capacity was decreased to about 85 percent of normal, and heart rate and blood pressure were unchanged from baseline. Breathing was entirely unassisted. Fluctuations in level of paralysis during a session produced influences on our results that were small relative to the size of the main effects. Glycopyrrolate (0.4 mg) was administered before curare to reduce autonomic effects; neostigmine was used to reverse the paralysis. Ptosis and diplopia were present throughout and subjects only viewed monocularly (the other eye was occluded by an eyepatch). Human Subject committees at both Columbia University and the University of Pennsylvania approved the protocols and procedures. The experiments were carried out at the anesthesiology department of the University of Pennsylvania Medical School.
3. The fixation target used in a number of experiments was a transilluminated "E" (24 by 24 minutes of arc, visual angle) that appeared indistinct or totally unresolvable when viewed with peripheral vision at more than 2° to 4° off central fovea. Thus, although we did not monitor eye position directly, we were well informed regarding whether or not foveal fixation was at least roughly maintained when required. Good foveal fixation was maintained throughout all measurements reported here. Each of the five other movable visual targets was a transilluminated circular disk, 9 minutes of arc in diameter. All targets were viewed from a distance of 1.83 m.
4. Settings were made by the experimenter positioning a visual target on oral command (grunts) of the subject. In experiments involving auditory targets an adaptive psychophysical procedure was used in which the experimenter switch-controlled the loudspeaker location from an adjacent room in response to pushbutton signals by the subject until the subject indicated that a sound-to-light localization match was reached (reliability of the match setting was 2°). When the subject was too weak to depress the pushbuttons, a second experimenter (always in the room with the subject) depressed the pushbuttons in response to oral commands by the subject.
5. Each of the sets of measurements described herein were carried out on at least the two observers L.M. and J.S.; in most cases all five observers were examined. The main features described for each type of measurement were consistent for all observers.
6. When the visual field was illuminated, the subject viewed the target, then closed his eyes, and finally pointed at the previously viewed target with eyes closed. Although our procedure for measuring the direction of finger pointing was not extremely accurate, it is clear that errors of the subject in this condition were no more than 2° to 3°.
7. Since the muscles guiding the finger were substantially weakened, the essential accuracy with which observers pointed to the horizontal in darkness implies that an inflow source is involved in sensing finger orientation; this must be in addition to whatever contribution is made by the vestibular organs.
8. Any small contribution to our results due to modification of neck and trunk proprioception by curare is below the level of precision of our measurements. It is unlikely that either the vestibular system or the inner ear (efferents as well as afferents)—both lying within the blood-brain barrier—were affected at all [see R. Klinke and N. Galley, *Physiol. Rev.* **54**, 316 (1974); P. S. Guth, C. H. Norris, R. P. Bobbin, *Pharmacol. Rev.* **28**, 95 (1976)]. In a study in which an increase in the sensitivity for detecting curare in cerebrospinal fluid was achieved by radioimmunoassay, only infinitesimal amounts were reported to pass the blood-brain barrier [R. S. Matteo, E. K. Pua, H. J. Khambatta, S. Spector, *Anesthesiology* **46**, 396 (1977)]; previous less sensitive methods had not detected any passage at all.
9. A separate psychophysical procedure (name-the-speaker) provides strong evidence that curare does not induce errors in auditory localization: The 25 loudspeakers were sequentially numbered and the observer in total darkness reported the speaker number on a series of trials in which order of presentation of the speakers was random. The observer's accuracy was not influenced by paralysis.
10. Although curare does not reach the inner ear or higher reaches of the auditory nervous system [see (*8*)], it does reach the tympanic and stapedius muscles in the middle ear (which lie outside the blood-brain barrier) and produces a diminution of the acoustic reflex [R. Smith, M. Loeb, J. L. Fletcher, D. M. Thomas, *Acta. Oto-Laryngol.* **62**, 101 (1966); R. A. Ruth, M. E. Johns, T. J. Gal, *Ann. Otol. Rhinol. Laryngol.* **89**, 188 (1980)], a result that is likely to be bilaterally symmetric and hence unimportant for the present purposes.
11. The auditory stimulus was a 64-cycle segment of a sine wave periodically repeated three times a second. To eliminate any possible localization cues that might originate in differences between loudspeakers, the frequency of the sine wave was quasi-randomly varied from trial to trial between 2 and 4.5 kHz (no significant effects of frequency on the localization match occur in this range); the duration of each burst was thus quasi-randomly varied between 14 and 32 msec.
12. This conclusion is most clearly drawn by noting that for two different gaze directions the error in auditory-to-visual matches may differ by 50°, implying a difference in error of EEPI of about 50°; nevertheless, in the presence of a structured visual field for both gaze directions visual localization (that is, perceived median plane and eye-level-horizontal settings) is accurate.
13. For a detailed discussion of the paradox, see L. Matin, J. Stevens, E. Picoult, in *Spatially Oriented Behavior*, A. Hein and M. Jeannerod, Eds. (Springer-Verlag, New York, 1982).
14. Under curare visual capture continued to function normally for other auditory stimuli (for example, when the experimenter spoke, the partially paralyzed subject who viewed him with eccentric gaze heard the speech as emanating from the experimenter's mouth). Thus it was our procedure for presenting stimuli that eliminated visual capture of the auditory stimuli emanating from the loudspeakers, not the curare.
15. J. K. Stevens, R. C. Emerson, G. L. Gerstein, T. Kallos, G. P. Neufeld, C. W. Nichols, A. C. Rosenquist, *Vision Res.* **16**, 93 (1976); G. S. Brindley, G. M. Goodwin, J. J. Kulikowski, D. Leighton, *J. Physiol. (London)* **258**, 65P (1976); R. Siebeck, *V. Graefes Archiv. Ophthalmol.* **155**, 26 (1954).
16. Supported by NIH grant EY 03198 and award N62269-80C-0296 from the Naval Air Development Center. A description of these experiments was presented at the 1980 meeting of the Association for Research in Vision and Ophthalmology in Orlando, Fla. [April Supplement to *Invest. Ophthalmol. Vis. Sci.* **19**, 81 (Abstr.) (1980)].

* Present address: Yale University Medical School, New Haven, Conn. 06520.
† Present address: University of Illinois Medical School, Chicago 60680.

27 January 1981; revised 2 November 1981

Plant Phenols Utilized as Nutrients by a Phytophagous Insect

Abstract. *Phenols are commonly regarded as feeding deterrents for phytophagous insects, but the tree locust* Anacridium melanorhodon *survives better and grows faster when certain phenols are added to a food plant that is relatively low in both protein and phenols. The phenols are at high concentration in the common host plants. Much of the phenol retained by the insect becomes bound in the cuticle where it probably stabilizes the protein.*

Plant phenols are commonly regarded as allelochemicals that are deterrent or deleterious to phytophagous insects (*1*). Tannic acid, however, has been shown to improve growth of the tree locust *Anacridium melanorhodon* (Walker) (*2*). Since tannic acid is hydrolyzed in the gut of locusts to gallic acid (*3*), the growth of nymphs was examined by feeding lettuce with and without the addition of gallic acid or related phenols found in host plants.

The lettuce leaves contained approximately 20 percent protein and 0.2 percent phenols (dry weight) (*4*), and the major phenols present were caffeic, protocatechuic, and gentisic acids. Phenols were added by dipping lettuce in alcoholic solutions of protocatechuic acid, gallic acid, ferulic acid, or caffeic acid. After evaporation of the solvent, measured quantities of leaf material with known weights of added phenol were fed to insects for the last two nymphal instars. Addition of protocatechuic, gallic, or caffeic acids significantly increased the survival and growth rates above that of the controls, whereas addition of ferulic

0036-8075/82/0409-0201$01.00/0

Table 1. Relative growth rate in fifth-instar nymphs and overall mortality in fifth- and sixth-instar nymphs of insects given lettuce with and without added phenol. Relative growth rate is measured as the increase in dry weight per unit insect weight (averaged over the instar) per day. All experiments were carried out at a photoperiodic cycle of 16 hours of light and 8 hours of darkness, and temperatures of 37°C during the day and the 28°C at night.

Diet	Number of insects	Relative growth rate	P (difference from controls)	Mortality (%)
Lettuce controls	25	48.6 ± 6.2		60
Lettuce plus gallic acid	13	62.2 ± 2.0	<.001	21
Lettuce plus protocatechuic acid	9	70.0 ± 8.0	<.001	22
Lettuce plus caffeic acid	16	58.9 ± 3.2	<.01	20
Lettuce plus ferulic acid	7	38.8 ± 4.8	<.05	90

Table 2. Percentage of carbon-14 recovered from tissues, feces, and carbon dioxide after ingestion of [^{14}C]gallic acid by five late-sixth-instar nymphs.

Source	Carbon-14 recovered (%)				
	Insect 1	Insect 2	Insect 3	Insect 4	Insect 5
Feces	78.5	90.9	64.7	78.6	68.1
Gut	10.1	4.9	29.1	10.1	20.3
Integument	6.3	2.3	3.0	8.6	7.3
Carbon dioxide	4.5	1.3	1.7	1.2	2.9
Hemolymph	0.3	0.1	1.3	1.4	1.0
Fat	0.2	0.4	0.1	0.5	0.3
Muscle	0	0	0.1	0	0

acid slightly reduced survival and growth rates (Table 1).

Since ferulic acid was ineffective in improving growth, a general action against pathogenic organisms in the gut seems unlikely. Moreover, there were no differences in the population sizes of the gregarine Protozoa or of Gram-staining material in the guts of control and treated insects (*5*). Thus, some physiological advantage of the phenols (other than ferulic acid) was assumed, and the fate of ingested labeled gallic acid was examined.

[^{14}C]Gallic acid was isolated from the leaves of *Geranium endressi* that had been fed [U-^{14}C]glucose for 24 hours (*6*). The labeled gallic acid was fed to individual insects, and no more food was given during the next 24 hours. The insects were then killed, and the expired carbon dioxide, the excreted feces, and the dissected tissues were prepared for scintillation counting (*7*). Despite considerable variability from insect to insect, the highest proportion of the label remaining in the body was recovered from the gut, much of it from the gut juices, although no solid food remained. The highest proportion absorbed from the gut was in the integument (Table 2), which had a specific activity (based on dry weight) that was more than four times that of any other tissue. A methanol extraction of the integument before oxidation indicated that only a relatively small proportion remained unbound. These results suggested a preferential deposition of labeled material in the cuticle.

The sclerotized exoskeletons of insects often form a very large proportion of the dry body weight and have a considerable phenol requirement (*8*). They utilize various tyrosine-derived 3,4-dihydroxyphenols in stabilization of the cuticle (*9*), and the buildup of ^{14}C in the integument of *A. melanorhodon* fed on [^{14}C]gallic acid indicates that this phenol, or a derivative of it, is utilized by this species. In view of the enhanced growth of this insect when a low-phenol, low-protein diet was supplemented with gallic acid (3,4,5,-trihydroxyphenol) or with protocatechuic and caffeic acids (3,4-dihydroxyphenols), we suggest that this insect can use a variety of such dietary phenols in the cuticle stabilization process. The ineffectiveness of ferulic acid is consistent with this suggestion, since it is hydroxylated only in position 4. Similarly enhanced growth occurred in *Bombyx mori* larvae when several phenols, including gallic acid or protocatechuic acid, were added to the artificial diets (*10*). There is also evidence that phenolic acids stimulate feeding in a number of phytophagous insect species (*11*), although behavioral tests with *A. melanorhodon* did not indicate that gallic acid acted as a phagostimulant in this species.

If *A. melanorhodon* can make use of dietary phenols in the sclerotization of cuticle, amino nitrogen would be conserved, since tyrosine would not be necessary to provide phenolic compounds for quinone formation before the cross-linking of protein molecules in cuticle stabilization. This would represent a most useful adaptation, since the host plants of the species are usually acacias and other desert trees and shrubs (*12*) that are commonly low in protein (*13*) although phenols are freely available. Samples of *Acacia* leaves from known host plants in northern Nigeria were analyzed and found to contain up to 2 percent simple phenols and only 15 percent protein (dry weight) (*14*). The phenols contained in the leaves included all four of the test chemicals.

Insects feeding on high-protein diets do not need to conserve amino nitrogen; therefore, the tyrosine pathway can provide the phenols needed for the cuticle. However phytophagous insects feed on plants that are often low in protein—which is most commonly limiting in their diet, particularly of tree feeders (*15*)—although phenols are readily available (*16*). Insects with such diets might be expected to have adapted to utilize plant phenols, and the evidence from *A. melanorhodon* and *B. mori* shows that these two species have so adapted.

There are few examples of insects utilizing proven allelochemicals as nutrients from their host plants. Certain bruchid beetles that feed on legume seeds containing the generally toxic canavanine are able to utilize this unusual amino acid as a source of nitrogen (*17*). Our work shows that phenols too may reduce the requirement for amino nitrogen, the saving in aromatic amino acids representing a considerable quantity of food protein.

E. A. BERNAYS
S. WOODHEAD
Centre for Overseas Pest Research, College House, Wrights Lane, London W8 5SJ, England

References and Notes

1. D. A. Levin, *Annu. Rev. Ecol. Syst.* **7**, 121 (1976); P. P. Feeny, in *Biochemical Interactions between Plants and Insects*, L. E. Gilbert and P. H. Raven, Eds. (Plenum, New York, 1975).
2. E. A. Bernays, D. J. Chamberlain, P. McCarthy, *Entomol. Exp. Appl.* **28**, 158 (1980).
3. E. A. Bernays, *ibid.* **24**, 244 (1978); ——— and D. J. Chamberlain, *J. Insect Physiol.* **26**, 415 (1980).
4. Total nitrogen was measured in air-dried leaf material (50 mg) by the micro-Kjeldhal method, and protein was estimated by multiplying the nitrogen value by 6.25. Total phenolics were measured with the Folin method, and qualitative analysis with thin-layer chromatography was confirmed by comparison of ultraviolet spectrums with those of authentic samples.
5. Insects were dissected at death or at the end of experiments, and counts made of gregarines in the gut. Smears were examined after being stained with Gram stains.
6. E. A. Bernays and S. Woodhead, *J. Insect Physiol.*, in press.
7. Nymphs of *A. melanorhodon* that had complet-

ed more than half of the sixth instar (postapolysis) were fed small sucrose-impregnated glass fiber disks to which [^{14}C]gallic acid (up to 100,000 disintegrations per minute) in methanol had been added; 20 to 100 percent of the disk was consumed in 2 to 6 hours. The insects were then sealed in test chambers (30°C) for 24 hours without food. At the end of the period the insects were killed. Hemolymph samples were taken for counting, and the total hemolymph volume was estimated. The tissue samples, and the fecal pellets produced over the period, were dried in cellulose thimbles, oxidized, and counted in a liquid scintillation counter (Packard Tri-Carb 2660). The expired carbon dioxide was collected as carbamate in phenylethylamine through which air was drawn from the test chambers during the period of the experiment; this was also used for measuring labeled carbon dioxide.

8. A. C. Neville, *The Biology of the Arthropod Cuticle* (Springer-Verlag, Berlin, 1975).
9. S. O. Andersen, *Insect Biochem.* **1**, 157 (1971).
10. M. Kato, *Entomol. Exp. Appl.* **24**, 485 (1978).
11. E. A. Bernays, *Ecol. Entomol.* **6**, 353 (1981); R. J. Heron, *Can. J. Zool.* **43**, 247 (1955); T. H. Hsiao and G. Fraenkel, *Ann. Entomol. Soc. Am.* **61**, 485 (1968).
12. G. Popov and M. Ratcliffe, *Anti-Locust Mem.* **9** (1968), entire volume.
13. National Academy of Sciences, *Tropical Legumes: Resources for the Future* (1979).
14. Leaves of *Acacia senegal* and *Acacia albida* were collected by C. Strudwick near Maidugeri, Nigeria, and sun-dried before being sent to England. Analysis was as in (*4*).
15. W. J. Mattson, *Annu. Rev. Ecol. Syst.* **11**, 119 (1980).
16. R. D. Gibbs, *Chemotaxonomy of the Flowering Plants* (McGill-Queen's Univ. Press, Montreal, 1974).
17. G. A. Rosenthal, D. L. Dahlman, D. H. Janzen, *Science* **192**, 256 (1976); G. A. Rosenthal, D. H. Janzen, D. L. Dahlman, *ibid.* **196**, 658 (1977).
18. We thank N. Jago for *Anacridium melanorhodon* adults, the Royal Botanic Gardens, Kew, for the *Geranium endressi*, C. Strudwick for collection of *Acacia* leaves, D. J. Chamberlain for assistance, and R. F. Chapman for criticism and encouragement.

5 January 1982

Modulation of Spasticity: Prolonged Suppression of a Spinal Reflex by Electrical Stimulation

Abstract. *Electrical subcutaneous nerve stimulation of radial, median, and saphenous nerves has been shown to produce prolonged analgesia. In a double blind study, such stimulation also suppressed clonus for 3 hours after stimulation ceased in subjects with spasticity. Since the effect is contralateral, each subject was his own control. Because stimulation of the nerve in the wrist suppressed ankle clonus, the mechanism mediating the effect must be centrifugal inhibition. These results suggest that subcutaneous nerve stimulation may also be a tool in the management of spasticity.*

Evidence for a gating mechanism in the spinal cord that modulates nociception (*1*) provides the rationale for the clinical practice of epidural spinal cord stimulation for pain relief (*2*). Several workers have observed that this procedure also benefits subjects with spastic paraparesis in that it increases voluntary muscle control, reduces rigidity, and improves bladder function (*3*). Thus, the same procedure can be used to alleviate pain and depress spasticity. As an alternative to spinal cord stimulation, we have studied the effects of subcutaneous nerve stimulation (SCNS) for the treatment of pain (*4*). We now report that the same treatment produces depression of spinal reflex excitability as demonstrated by prolonged and complete suppression of clonus. Preliminary reports of these results have appeared elsewhere (*4*) and have been documented on film.

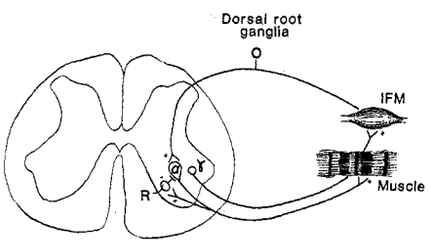

Fig. 1. Partial diagram of the basic stretch reflex. Stretching of intrafusal muscle (*IFM*) produces firing of stretch receptor which has its cell body in the dorsal ganglion. Activation of the stretch receptor results in firing of alpha motoneurons, which in turn produces muscle contraction and decreases activity of the stretch receptor of the IFM. The axon of the alpha motoneuron sends a collateral to a Renshaw cell (*R*) which inhibits the homonymous alpha motoneuron. The sensitivity of the stretch receptor is also regulated by gamma efferents, which are under bulbospinal control. Multiple inhibitory and excitatory factors regulate the output of the alpha motoneuron preventing the cyclic discharge that produces clonus.

Clonus is a 5- to 7-Hz pathological oscillation exhibited by spastic muscle after being passively stretched. After initial tendon jerk, the muscle relaxes and stretches the muscle spindles. Stretch produces a synchronous resumption of spindle afferent discharge. Figure 1 depicts the mechanism underlying the basic stretch reflex. Synchronous increased monosynaptic projection of spindles causes homonymous alpha motoneurons to discharge again, producing a second reflex contraction of the muscle. In neurologically intact spinal cord, input from muscle spindles is insufficient to initiate cyclical alpha motoneuron discharge. In spastic muscles, however, hyperexcitability of the alpha or gamma motoneurons is such that synchronous spindle firing produces cyclic alpha motoneuron firing and produces reflex contractions. Such a closed oscillating feedback loop indicates the importance of inhibitory control mechanisms that normally promote asynchrony of neural activity.

Subjects were pain-free patients in the multiple sclerosis clinic or on the neurosurgery ward at the UCLA Center for Health Sciences. Nine patients had multiple sclerosis, four had postlaminectomy irritability, and all had ankle clonus that persisted for 40 to 60 beats when triggered by patellar stretch.

The SCNS was delivered by subcutaneous placements of 30-gauge stainless steel needles in the median and radial nerves 5 cm proximal to the wrist flexure and in two points along the route of the saphenous nerve—at the metatarsal cuneiform junction and below the medial malleolus. The needles were attached to an electrical output (TA 4 stimulator), which delivered 20-Hz spike wave stimulation. The intensity of the current was increased gradually until it reached about 200 μA.

Correct placement of needles in the median and radial nerves was verified by reports of sensation of vibration along the distribution of each nerve. Stimulation of the saphenous nerve was frequently accompanied by a massive efferent outflow consisting of clonus, fanning of the toes, and occasional stepping movements. In normal subjects, stimulation of this nerve produced barely visible muscle twitches. Gross movements, which could be produced only in spastic patients, were presumably reflections of heightened neural irritability. In all cases, peripheral stimulation was accompanied by erythema (a reddening of surrounding tissue) and local elaboration of sympathetic signs, such as sweating, coldness, and piloerection.

Subjects were given SCNS or control SCNS (which consisted of stimulation of points distal from the three peripheral

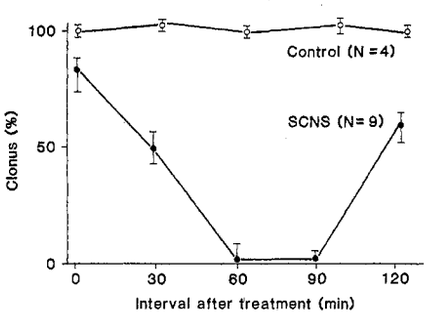

Fig. 2. Time course for inhibition of clonus by SCNS. Subjects were given SCNS or placebo, which consisted of electrical stimulation of distal points. Clonus was measured as a percentage of contractions before treatment.

0036-8075/82/0409-0203$01.00/0