hold the skin sample at constant width, it does not show that the skin stores any energy at all. Shark skin is oriented on the shark like cloth cut on the bias. Alternate layers of collagen fibers wind around the fish's body in helices of opposite hand. Stretching such a skin longitudinally will make it shrink laterally. Most of the energy put into the skin by stretching it lengthwise may be passed on by the skin to the lateral restraints as it pulls them together. The apparent rise in stiffness with lateral tension may mean only that more work is being done on the lateral restraints. To find the energy stored in the skin in this experiment the authors would have had to record the lateral force-extension curve and subtract the area under it from that under the longitudinal force-extension curve.

The ability of the skin to store energy should depend mostly on the compliance of its collagen fibers, which, as Wainwright *et al.* (1) state, are very stiff in tension. Experiments in which the skin was stretched parallel to one set of fibers confirm this high stiffness (2) and show that most of the energy represented by the area under the force-extension curves described in (1) could not have been stored in the skin.

I have not observed sharks much, but in other fish the pattern of swimming motion is nearly independent of speed. To go faster the fish uses the same pattern of motion, but does it faster. Kinetic energy involved in this motion goes as $(\text{speed})^2$, and so should any potential energy stored in springs if the same pattern of forces and motion is to be maintained. Ordinary springs do not have this property (3). In the experiments of Wainwright *et al.* (1) the skin appears to be a modulatable spring, but, as shown above, this apparent property is most likely a wrong interpretation of the experiment.

C. W. McCutchen
Laboratory of Experimental Pathology,
National Institute of Arthritis,
Metabolism, and Digestive Diseases,
Bethesda, Maryland 20205

References

1. S. A. Wainwright, F. Vosburgh, J. H. Hebrank, *Science* **202**, 747 (1978).
2. S. A. Wainwright, personal communication.
3. C. W. McCutchen, *J. Biomech.* **3**, 271 (1970).

18 December 1978

If stiffness is considered to be the resistance to extension, then our figure 2 (1) shows that the stiffness of shark skin varies with stress in the skin due to restraining force. Since the pressure under the skin varies with the swimming speed, so therefore do the restraining force, skin stress, and stiffness of the skin in a swimming shark: we find no reason to alter our conclusions. We are unable to draw the same range of conclusions from McCutchen's comment and his work on trout that he has drawn.

S. A. Wainwright
F. Vosburgh
J. H. Hebrank
Zoology Department, Duke University,
Durham, North Carolina 27706

References

1. S. A. Wainwright, F. Vosburgh, J. H. Hebrank, *Science* **202**, 747 (1978).

31 December 1979

Lateralized Cognitive Processes and the Electroencephalogram

Many investigators have found differences in the balance of electroencephalographic (EEG) activity between the two hemispheres during tasks which differentially require verbal as opposed to spatial processing. Such results have been interpreted as reflecting differences in hemispheric utilization for particular cognitive processes. Gevins *et al.* (1) have challenged this interpretation by pointing out that putatively left- and right-hemisphere tasks often differ not only in their cognitive demands, but also in their "stimulus characteristics, efferent activities (limb and eye movements), and performance-related factors (task demands and a subject's ability and effort)."

We believe that this contention is not strongly supported by their data (1) and is seriously challenged by a large body of data, much of which they did not cite. At least nine studies have reported significant differences in relative hemispheric activation in the predicted direction when the EEG was recorded in response to verbal and nonverbal stimuli and the subjects were not required to make any overt motor response (2, 3). Significant left and right differences have also been found in studies where response requirements for verbal and nonverbal tasks were equated (4–6). Asymmetries in EEG activity have also discriminated between purely covert verbal and nonverbal tasks (6, 7) involving no stimulus or response (6), thus rigorously satisfying the criteria of Gevins *et al.* (1) for controlling the three essential noncognitive aspects of task performance: stimulus characteristics, efferent activities, and performance-related factors.

In support of their contention that measures of EEG asymmetry do not reflect lateralized cognitive processes, Gevins *et al.* present the results of two studies. The results of the first study indicated that tasks could be differentiated on the basis of EEG laterality measures. A second experiment was performed to match more carefully tasks on "efferent components, stimulus characteristics, and performance-related factors." These tasks were of shorter duration (6 to 15 seconds each) than those in the first study (1 minute). We believe that the tasks chosen for the two experiments and the methods used contributed significantly to the negative outcome of the experiments and that definitive conclusions cannot be drawn from them. Although Gevins *et al.* found that the first 15-second segment discriminated between writing versus the Koh's block design task in experiment 1, the subjects' set would probably be quite different in this situation compared to that in experiment 2. It is not clear from their report whether Gevins *et al.* randomized tasks in experiment 2. The methods used in their two experiments differed significantly. The rapidity and possibility of random task presentation in experiment 2 might have prevented the subjects from adopting a consistent cognitive set. Moreover, the spatial task used by Gevins *et al.* in experiment 2 was different from the one used in experiment 1. Recent evidence indicates that the mental rotation task used in experiment 2 is associated with relative left-hemisphere activation in comparison with other spatial tasks where stimulus-, motor-, and performance-related factors were equated (8). Thus, in effect, Gevins *et al.* (1) may have been comparing the effects of three different "left hemisphere" tasks in experiment 2.

In sum, the results reported by Gevins *et al.* do not convincingly support their contention that EEG asymmetry is unaffected by cognitive differences among tasks. In their experiment 2, it is unclear whether cognitive differences did indeed exist among the tasks. Moreover, their study must be viewed in the context of many other studies in which noncognitive sources of variance have been controlled and significant differences in EEG asymmetry between left and right hemisphere tasks have been found. As Gevins *et al.* have indicated, there is clearly a need to consider a variety of frequency spectra since the assumption that the EEG moves to a higher frequency band when the spectral intensity of the α band is attenuated during active tasks may not always be legitimate. The data of Gevins *et al.* should encourage further studies of the multiple dimensions along which cognitive tasks may vary and the relations of these tasks to changes in particular features of the EEG spectral signature.

Richard J. Davidson
Department of Psychology,
State University of New York,
Purchase 10577

Howard Ehrlichman
Department of Psychology,
City University of New York
Graduate Center, New York 10036

References and Notes

1. A. S. Gevins, G. M. Zeitlin, J. C. Doyle, C. D. Yingling, R. E. Schaffer, E. Callaway, C. L. Yeager, *Science* **203**, 665 (1979).
2. L. R. Warren, L. Peltz, E. S. Haueter, *Brain Language* **3**, 283 (1976); J. G. Beaumont, A. R. Mayes, M. D. Rugg, *Electroencephalogr. Clin. Neurophysiol.* **45**, 393 (1978).
3. J. C. Doyle, R. Ornstein, D. Galin, *Psychophysiology* **11**, 567 (1974); S. R. Butler and A. Glass, *Electroencephalogr. Clin. Neurophysiol.* **36**, 481 (1974); K. Osborne and A. Gale, *Biol. Psychol.* **4**, 185 (1976); J. E. Bennett and J. Trinder, *Psychophysiology* **14**, 293 (1977); S. S. McLeod and L. J. Peacock, *ibid.*, p. 308; M. Hirshkowitz, J. Earle, B. Paley, *Neuropsychologia* **16**, 125 (1978); R. J. Davidson and A. Marshak, *Psychophysiology* **15**, 269 (1978).
4. R. J. Davidson and G. E. Schwartz, *Psychophysiology* **14**, 58 (1977).
5. G. McKee, B. Humphrey, D. W. McAdam, *ibid.* **10**, 441 (1973); W. Rapaczynski and H. Ehrlichman, in preparation.
6. K. I. Robbins and D. W. McAdam, *Brain Language* **1**, 189 (1974).
7. H. Ehrlichman and M. S. Wiener, *Psychophysiology*, in press.
8. R. Ornstein, J. Johnstone, J. Herron, C. Swencionis, *Neuropsychologia*, in press.

11 October 1979

In two experiments we found many spatial EEG patterns, including interhemispheric ones, which distinguished uncontrolled tasks (experiment 1), but none that distinguished controlled tasks (experiment 2) (*1*). We concluded that the existence of spontaneous EEG patterns specifically correlated with the mental components of tasks had not been demonstrated (*2*).

Davidson and Ehrlichman make three points: (i) Many previous studies have found "left-right" EEG differences related to "cognitive set" under supposedly controlled conditions; (ii) the random occurrence of "short" duration (10 to 15 seconds) tasks in our experiment 2 precluded the formation of a cognitive set; and (iii) the mental rotation task (*3*) used in our experiment 2 is not a "right hemisphere" task.

We do not think that these points are substantive:

Controlled studies (see Table 1). None of the studies cited by Davidson and Ehrlichman meet all the minimum criteria necessary to rule out extraneous, other-than-mental influences on the EEG patterns recorded (see Table 1). In order to study possible EEG signs of mental operations, it is necessary that all of the following criteria be met (*4*).

Table 1. Methodological shortcomings of studies cited by Davidson and Ehrlichman. The criteria for experiments on EEG correlates of mental activities [1, 2, 4, 5 from Donchin *et al.* and 3 and 6 from Gevins and Schaffer, see (*4*)] described in the text.

Study	Fails to meet criteria*
Beaumont *et al.* (*18*)	3, 4
Bennett and Trinder (*19*)	1, 2, 3, 4, 5
Butler and Glass (*20*)	3, 4, 6
Davidson and Marshak (*21*)	2, 3, 5, 6?
Davidson and Schwartz (*22*)	1?, 2?, 3?, 4?, 5, 6?
Doyle *et al.* (*23*)	1, 2, 3, 4, 5
Ehrlichman and Wiener (*24*)	1, 2, 3, 4, 5, 6?
Hirshkowitz *et al.* (*25*)	3, 4, 5, 6
McKee (*26*)†	3, 4?, 5, 6
McLeod and Peacock (*27*)	1, 3, 4, 5
Ornstein *et al.* (*28*)	1, 3, 4, 6
Osborne and Gale (*29*)	1, 3, 4, 6
Robbins and McAdam (*30*)	3, 4, 6
Schwartz *et al.* (*31*)	3, 5, 6
Warren *et al.* (*32*)	3, 4, 6

*Items with question mark (?) denote insufficient data in report to evaluate. †Sample size was four.

1) There should be minimal or no differences between tasks in stimulus properties.

2) There should be no differences in efferent activities between tasks.

3) In order to minimize EEG differences associated with effort and task difficulty, there should be minimal or no differences in performance-related factors between tasks.

4) There should be behavioral validation that the tasks were correctly performed during the time corresponding to those segments of EEG recording selected for analysis (*5*).

5) The EEG patterns from the left and right hemispheres should be presented separately.

6) All extracerebral artifacts from the EEG should be rejected prior to analysis.

Cognitive set. EEG correlates of "cognitive set" have previously been reported for uncontrolled tasks 9 seconds in duration (*6*). Two results in our experiments tended to contradict the requirement of a cognitive set that takes longer than 15 seconds to establish. (i) In our experiment 1, EEG patterns associated with uncontrolled tasks were more consistently discriminable during the first 15 seconds than during any other portion of the 1 minute of task performance. (ii) In our experiment 2, when two or three mental rotation problems (each lasting 6 to 15 seconds) happened to occur in a row, there were no significant differences in any spectral EEG measure from any electrode placement between the first and subsequent problems.

Right hemisphere tasks. It is reasonable to suppose that the mental rotation task (*3*) used in our experiment 2 requires different cognitive operations from the addition and letter substitution tasks and that this task was associated with a spatial EEG pattern. These suppositions follow from three lines of evidence not involving the EEG. (i) The isolation of a spatial rotation factor, distinct from a number facility factor in factor-analytic evaluations of psychometric test batteries (*7, 8*). (ii) Shepard and his colleagues (*9*) found that practiced persons solve such tasks by constructing and rotating some sort of mental image. (iii) Neuropsychological evidence of deficits in spatial rotation abilities from patients showing right posterior cortical lesions (*10*) or from commissurotomy patients whose left hemisphere only was used during task performance (*11*). Although patients with left parietal lesions also display deficits in spatial rotation ability (*12*), the relative loss in ability seems greater for right hemisphere damage (*13*).

Thus, using equal or more rigorous criteria for the selection of cognitively and cortically differentiated tasks than those customarily employed in previous EEG research, we expected the mental rotation task to be more right hemisphere oriented than the arithmetic and letter substitution tasks. We did not find any EEG spectral differences between tasks. Since our analytic methodology is demonstrably more powerful than that used in previous EEG studies on this topic (*14*), the negative result may not be attributed to weakness of the analysis. We therefore do not accept the conclusions of non "right hemisphericity" by others who have used the mental rotation task without meeting all criteria 1 through 6 (*15*). Additionally, some studies not meeting criteria 1 through 6 have shown relative right hemisphere activation for this same mental rotation task (*16*).

Thus, it is unreasonable to dismiss a posteriori as not "right hemisphere" a task that fails to show a desired effect in the EEG. To do so would imply that the EEG is an accurate measure of higher cortical functions, but this is exactly the hypothesis being tested.

Over the last 50 years, researchers have frequently thought they had evidence relating EEG patterns to mental activities, only to find that their conclusions were unwarranted because of inadequate controls or insufficiently sensitive analysis (*17*). Our negative results pin down the inadequacies of the current research paradigm that attempts to correlate abstract psychological constructs with simple measures of the mass electrical activity of the nervous system.

ALAN S. GEVINS, JOSEPH C. DOYLE
ROBERT E. SCHAFFER
ENOCH CALLAWAY
CHARLES YEAGER

*EEG Systems Laboratory, Langley
Porter Institute, University of
California School of Medicine,
San Francisco 94143*

References and Notes

1. A. S. Gevins, G. M. Zeitlin, J. C. Doyle, C. D. Yingling, R. E. Schaffer, E. Callaway, C. L. Yeager, *Science* **203**, 665 (1979).
2. The term spontaneous EEG does not include event-related (time-locked) brain potentials (ERP's).
3. R. N. Shepard and J. Metzler, *Science* **171**, 701 (1971).
4. These criteria were discussed by E. Donchin, M. Kutas, and G. McCarthy [in *Lateralization in the Nervous System*, S. Harnad, R. Doty, L. Goldstein, J. Jaynes, G. Krauthamer, Eds. (Academic Press, New York, 1977), p. 339] and A. S. Gevins and R. E. Schaffer (*17*).
5. This includes eliminating tasks that by common sense can be expected to be beyond the abilities of the participants such as mentation for up to 40 seconds without internal vocalization.
6. K. Osborne and A. Gale, *Biol. Psychol.* **4**, 185 (1976).
7. L. Thurstone, *Multiple Factor Analysis, a Development and Expansion of "The Vectors of Mind"* (Univ. of Chicago Press, Chicago, 1947).
8. J. French, R. Ekstrom, L. Price, *Kit of Reference Tests for Cognitive Factors* (Educational Testing Service, Princeton, N.J., 1963); J. Carroll, in *The Nature of Intelligence*, L. Resnick, Ed. (Erlbaum, Hillsdale, N.J., 1976).
9. L. Cooper and R. Shepard, in *Handbook of Perception*, vol. 8, *Space and Object Perception*, E. Carterette and M. Friedman, Eds. (Academic Press, New York, 1978); M. Just and P. Carpenter, *Cognitive Psychol.* **8**, 441 (1976).
10. H. Hecaen, in *Interhemispheric Relations and Cerebral Dominance*, V. Mountcastle, Ed. (Johns Hopkins Press, Baltimore, 1962); J. Bogen, *Bull. L.A. Neurol. Soc.* **34**, 135 (1969).
11. J. Levy-Agresti and R. Sperry, *Proc. Natl. Acad. Sci. U.S.A.* **61**, 1151 (1968); B. Milner and L. Taylor, *Neuropsychologia* **10**, 1 (1972).
12. N. Butters and M. Barton, *Neuropsychologia* **8**, 205 (1970); D. Benson and M. Barton, *Cortex* **6**, 19 (1970).
13. M. Piercy, H. Hecaen, J. De Ajuriaguerra, *Brain* **83**, 225 (1960); E. DeRenzi, in *Asymmetrical Function of the Brain*, M. Kinsbourne, Ed. (Cambridge Univ. Press, Cambridge, 1978), p. 49; R. Nebes, in *ibid.*, p. 99.
14. This was evident in the results of experiment 1, in which we were able to predict the behavioral task from independent EEG samples [A. S. Gevins, G. M. Zeitlin, C. D. Yingling, J. C. Doyle, M. F. Dedon, J. H. Henderson, R. E. Schaffer, J. T. Roumasset, C. L. Yeager, *Electroencephalogr. Clin. Neurophysiol.* **47** (No. 5), 693 (1979); A. S. Gevins, *IEEE Trans. Pattern Anal. Machine Intell.*, in press.
15. In a recent study, R. Ornstein *et al.* (*Neuropsychologia*, in press) included a modified version of the mental rotation task and produced results consistent with our negative finding. However, their study did not meet methodological criteria 1, 3, 4, and 6 outlined above. In particular, their EEG and behavioral evidence indicated that participants made relatively less effort for this task.
16. C. Furst, *Nature (London)* **260**, 254 (1976); C. Robert and D. Low, *Electroencephalogr. Clin. Neurophysiol.* **44**, 724 (1978).
17. A. S. Gevins and R. E. Schaffer, *CRC Crit. Rev. Bioeng.*, in press.
18. J. G. Beaumont, A. R. Mayes, M. D. Rugg, *Electroencephalogr. Clin. Neurophysiol.* **45**, 393 (1978).
19. J. E. Bennett and J. Trinder, *Psychophysiology* **14**, 293 (1977).
20. S. R. Butler and A. Glass, *Electroencephalogr. Clin. Neurophysiol.* **36**, 481 (1974).
21. R. J. Davidson and A. Marshak, *Psychophysiology* **15**, 269 (1978).
22. R. J. Davidson and G. Schwartz, *ibid.* **14**, 58 (1977).
23. J. C. Doyle, R. Ornstein, D. Galin, *ibid.* **11**, 567 (1974).
24. H. Erlichman and M. Wiener, *ibid.* **16**, 247 (1979).
25. M. Hirshkowitz, J. Earle, B. Paley, *Neuropsychologia* **16**, 125 (1978).
26. G. McKee, B. Humphrey, D. W. McAdam, *Psychophysiology* **10**, 441 (1973).
27. S. S. McLeod and L. J. Peacock, *ibid.* **14**, 308 (1977).
28. R. Ornstein *et al.*, *Neuropsychologia*, in press.
29. K. Osborne and A. Gale, *Biol. Psychol.* **4**, 185 (1976).
30. K. I. Robbins and D. W. McAdam, *Brain Language* **1**, 189 (1974).
31. G. Schwartz, R. Davidson, E. Pugash, *Psychophysiology* **13**, 498 (1976).
32. L. R. Warren, L. Peltz, E. S. Haeuter, *Brain Language* **3**, 283 (1976).

11 December 1979

Differential Killing of Normal and Cystic Fibrosis Fibroblasts by Dexamethasone

Kurz *et al.* (*1*) claimed that neither dexamethasone nor dibutyryl adenosine 3′,5′-monophosphate (cyclic AMP) kills normal human diploid fibroblasts. This contradicts our previous finding that the two drugs reduce the plating efficiency of normal human diploid fibroblasts but are less toxic to fibroblasts from individuals with cystic fibrosis (CF) (*2*–*6*). Although Kurz *et al.* claimed to have reproduced our methods, there were serious differences which render their results invalid.

In our studies, we distinguished between normal and CF fibroblasts through the use of a cell survival assay. This assay requires that each cell, in order to be scored as a survivor, express its reproductive capacity by doubling at least six times after exposure to cytotoxic agents. The correct use of this method requires that stringent standards be adhered to in order to ensure that cells scored as survivors (in the form of colonies) are indeed capable of prolonged proliferation after exposure to a cytotoxic agent. In our earlier reports, we had stated that cells must form colonies of at least 50 cells (*2*), but that figure was later increased to 65 to 75 cells (*6*). To ensure that only true colonies were counted, cells in all our dishes are counted visually and then scanned under the microscope. Colonies found not to contain the minimum number of cells are excluded from the count.

When appropriate minimum standards are not adhered to in scoring colonies, invalid results are obtained since many cells are able to perform four or five divisions after exposure to a cytotoxic agent before reproduction ceases. When colonies of less than a certain number of cells are counted as survivors, the result is that the actual toxicity of a particular agent is underestimated. (Control dishes have few or no abortive colonies, whereas dishes exposed to cytotoxic agents, especially at high doses, have many abortive colonies. Therfore, when survival is corrected for plating efficiency, the result is falsely elevated.) Kurz *et al.*'s claim that 78 to 134 percent of normal fibroblasts survived in $10^{-5}M$ dexamethasone phosphate was based on counts of colonies that contained "about 30 or more cells." This would require only five cell doublings and thus would include a fair number of abortive colonies. We have seen many cells divide up to five times after drug exposure and then cease dividing as determined by daily microscopic observation. To illustrate the consequences of including abortive colonies in the analysis, we are providing data from an experiment with human cells that were exposed to ethylmethane sulfonate (EMS), a potent cytotoxic mutagen (Table 1). The effect of including small colonies is to make EMS seem less toxic than it actually is.

Another issue raised by Kurz *et al.* is the effect of cell number on the plating

Table 1. Cell survival after exposure to ethylmethane sulfonate.

Drug concentration	Cells plated per 100-mm dish	Colonies with ≥ 75 cells*	Survival† (%)	Colonies with ≥ 30 cells*	Survival† (%)
None	1500	54	100	57	100
50 μg/ml	2000	42	59	67	88
100 μg/ml	3000	46	43	97	85

*Numbers are averages. †Corrected for plating efficiency.