of the training period. This variable could be controlled by subjecting the control mothers to the same training and premating stress as the experimental mothers.

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I am grateful to A. R. Kaplan for pointing out a possible interpretation of my experimental results on prenatal influences [*Science* **125**, 698 (1957)] that I had been quite aware of but had neglected to indicate in the published article. I am now starting a project to examine this question thoroughly.

How such effects, if they really occur, have their action cannot be answered at present. But I would suggest that a mother stressed before pregnancy would tend to have a much lower threshold of reactivity to any of the mild stresses that may occur during the course of normal laboratory life. Thus, radically altering the mother before pregnancy may be quite equivalent to radically altering the environment during pregnancy.

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Electroencephalographic "Blocking" and "Adaptation"

Under the title "EEG, consciousness, and sleep," Simon and Emmons (*1*) have presented evidence that conditions of wakefulness favorable to recognition and recall of stimuli are accompanied or preceded within 30 seconds by recordable alpha rhythm. Yet the authors recognize that processes of attention or concentration following stimulation tend to be simultaneous with reduction or "blocking" of the alpha rhythm.

Although the electroencephalogram is a record, from outside the head, of electric activity in the underlying cortex, the magnitude of this activity depends to a very large extent on the effectiveness of subcortical pacemakers in driving and synchronizing the cortical cellular activity (*2*). It follows that the blocking of alpha by stimulation can be easily explained if it is assumed that, during reaction, the cortical cells engage in independent, nonsynchronous activity (*3*). However, recent evidence shows that, at least in the case of peripheral stimuli, blocking or "activation" of the cortex may be the result of asynchronous subcortical impulses to the cortex from the brain stem reticular formation (*4*). Whether this latter explanation applies equally to blocking by perceptual and ideational stimuli, which depend for effectiveness on cortical or cortico-thalamic integrative and interpretative processes, may still be a question.

Particularly significant is the fact that blocking occurs in response to any *new* stimulus that calls for interpretation or readjustment but disappears as the stimulus is evaluated and adjusted to. An example of decreased blocking by successive loud gong stimuli at 10-second intervals is presented in Fig. 1. Measurements of the "percent time alpha" (*5*) of 20 left occipital electroencephalographic records were obtained by conventional methods. The percentage of time occupied by sequences of three or more 8- to 12-per-second waves of more than 15 μv amplitude was determined for the 3 seconds before and the 3 seconds after each gong stimulus. The mean effects of nine successive repetitions for 20 subjects show a progressive reduction of blocking. The decrease of blocking from gong 1 to gong 6 is 16.02 percent, and from gong 1 to gong 9 is 28.12 percent. The probability of this decrease occurring by chance is less than 5 in 100 at gong 6 and less than 1 in 100 at gong 9.

Phase relationships of waves in different head areas had previously shown reliable adaptation of response to successive gong stimuli, and the palmar galvanic responses were likewise reliably reduced with repetition (*6*). We have also found that, with eyes closed, repeated writing of a word on an imaginary blackboard produces marked initial blocking, especially in the left hemisphere, and a decrease or elimination of blocking with practice. In fact, any novel stimulus or activity will tend, at first, to be accompanied by blocking of the alpha rhythm, and, with familiarity, habituation, solution of the problem, or rendering of the activity automatic, alpha will be restored.

Similar observations of blocking of the alpha rhythm are to be found throughout the literature on the electroencephalogram. Their import, however, is not always made explicit. That blocking occurs during periods of attention, adjustment, and problem solving, when cortical integrative processes are going on, and that alpha returns with "automation" as other mechanisms, presumably subcortical, become competent to carry on and free the cortex for new problems deserve consideration. As is possibly evident in Simon and Emmon's observation of the waking resting state, alpha may then prevail, and the cortex will ride the wave of mental operations as monitor—to intervene only when things in some department fail to run smoothly.

The possibility of a shift from blocking to alpha activity with repetition, from active integration to automation, and from, presumably, cortical to subcortical control with habituation accounts likewise for many puzzling observations. It explains, for example, the fact noted by Hebb (*7*) and others that complex test behaviors involving *learned* skills which are probably relegated to subcortical control may be relatively little disturbed by extensive cortical damage. It explains how complex psychomotor behaviors, which were once cortically determined, may sometimes become inaccessible and uncontrolled when routinized under automatic subcortical control. It explains Simon and Emmons' observation of a relatively high incidence of waking alpha during learning of repeated stimuli, notwithstanding the blocking effects usually associated with processes of attention or "concentration."

If the afore-noted electroencephalographic indications of the shifting levels

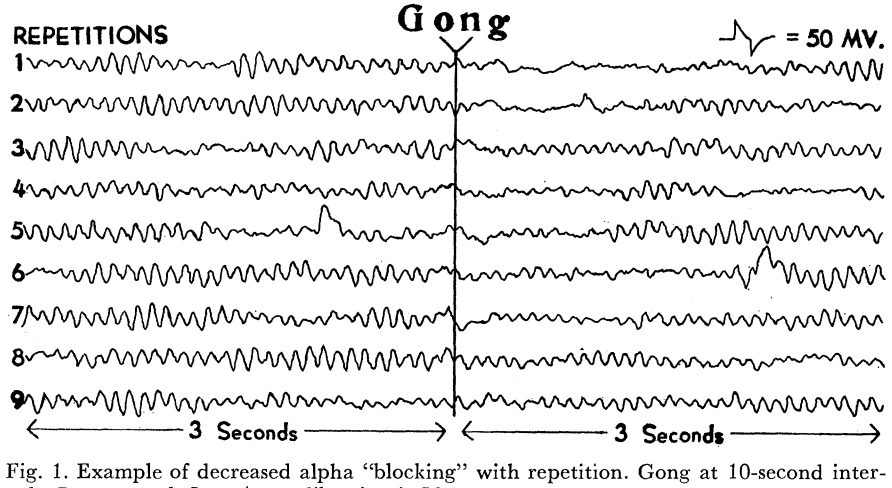

Fig. 1. Example of decreased alpha "blocking" with repetition. Gong at 10-second intervals. Paper speed, 5 cm/sec calibration is 50 μv.

of relative cortical-subcortical function are valid, they present far-reaching implications for the interpretation of cerebral function.

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References and Notes

1. C. W. Simon and W. H. Emmons, *Science* 124, 1066 (1957).
2. E. W. Dempsey and R. S. Morison, *Am. J. Physiol.* 135, 293 (1941).
3. E. Adrian, *Arch. Neurol. and Psychiat.* 32, 1125 (1934).
4. G. Moruzzi and H. Magoun, *Electroencephalog. and Clin. Neurophysiol.* 1, 455 (1949).
5. C. Shagass, *J. Exptl. Psychol.* 31, 367 (1942).
6. C. W. Darrow *et al.*, *Trans. Soc. Biol. Psychiat.* 11, 29 (1956). Also *J. Nervous Mental Disease*, 124, 38 (1956).
7. D. O. Hebb, *The Organization of Behavior* (Wiley, New York, 1949).
8. This study was supported, in part, by a grant from the Illinois Public Welfare Mental Health Fund.

4 April 1957

Differential Excretion of D-Phenylalanine in Man

In the course of an investigation into the extent of genetic control over certain aspects of phenylalanine metabolism in man, a major discrepancy was noted between the results of two methods used in determining urinary phenylalanine after ingestion of the L form of this amino acid. The two methods were one-dimensional paper chromatography, in which a butanol-acetic acid-water mixture was used, and a modified form of the decarboxylase method of Udenfriend and Cooper (*1*). The paper chromatographic results were markedly higher than the decarboxylase values and were well beyond any methodologic differences. Since the decarboxylase method is specific for L-phenylalanine, while chromatographic techniques do not distinguish between the L and D forms, the simplest explanation of these results was that the ingested phenylalanine was racemic. Consequently, tests were run to examine this hypothesis, and they clearly demonstrated that the original substrate was slightly racemic. The purpose of this report is to point out the possibility and implications of minor isomeric contamination in studies of amino acid metabolism and to consider the interesting variation in excretion rate of D-phenylalanine that was observed among individuals in these experiments (*2*).

Meister *et al.* (*3*) have discussed the problem of determining the degree of optical purity of various amino acids. They point out that techniques such as polarimetry cannot detect isomeric impurities of less than 1.00 mg percent, while the use of oxidases and decarboxylases in properly designed Warburg experiments can detect isomeric contamination of less than 0.10 mg percent. In this work, the presence of D-phenylalanine was demonstrated by measuring the oxygen uptake on incubation with D-amino acid oxidase, according to Burton (*4*). The original sample of phenylalanine was run in the Warburg apparatus with known amounts of D-phenylalanine as controls, and oxygen uptake occurred equivalent to 0.60 mg percent of D-phenylalanine. A second sample of L-phenylalanine from a different source, but not used in these metabolic experiments, was tested in a similar manner and was found to contain 0.17 mg percent of D-phenylalanine.

For most biochemical and physiological experiments, such minor impurities would probably be undetectable. However, in studies that involve recovery of ingested amino acids from the urine, isomeric contamination of the order of 0.10 mg percent could lead to serious error. This follows from the fact that the kidney acts as a highly selective filter, retaining most L-amino acids with an efficiency of more than 95 percent, while the D forms are excreted quite readily (*5, 6*).

In the present studies, 2 g of the L-phenylalanine, estimated to contain 0.60 mg percent of the D-isomer, was given orally, and urine was collected for the following hour. The phenylalanine concentration in the urine samples was determined by the decarboxylase and paper chromatographic methods, the difference between the two being taken as an estimate of the concentration of D-phenylalanine in the specimens. The percentage of the D-isomer in these specimens averaged more than 50 percent. With feedings of from 5 to 10 g of the substrate, isomeric contamination of as little as 0.10 mg percent could lead to an error of the same order of magnitude.

The simplest way to avoid the problem of minor isomeric contamination would be to utilize techniques that are specific for the L form of the amino acid, such as the enzymic, and most microbiological methods. Another approach would be to use the assays suggested by Meister *et al.* (*3*) to insure minimal isomeric contamination. In this connection we should like to suggest the possibility of using man as a concentrating mechanism for a suspected racemic amino acid mixture before assaying it for D contamination. Such a system could increase by 100-fold the sensitivity of detection of isomeric contamination.

In Table 1 are given the data on the excretion rate of D-phenylalanine after the ingestion of 2 g of the racemic phenylalanine, containing 0.60 mg percent of the D-isomer. The data are reported as milligrams of D-phenylalanine per milligrams of creatinine and represent the average concentration for the first hour's urine specimen following the feeding. The experimental subjects were normal monozygotic and like-sexed dizygotic twins.

As can be seen, there is considerable variation in the excretion rate of D-phenylalanine, the range being more than 15-fold (0.024–0.379). Variability in the excretion rate of D-isomers, and in particular of D-phenylalanine, has been observed before (*5, 7*). The physiologic ex-

Table 1. Urinary excretion rate of D-phenylalanine in monozygotic and dizygotic twins.

Twins	Sex	Ratio of D-phenylalanine to creatinine (mg/mg)	Intrapair differences	Mean intrapair difference
		Monozygotic		
1 A	♀	0.086	0.020	
B		0.106		
2 A	♀	0.091	0.026	0.025
B		0.117		
3 A	♂	0.052	0.028	
B		0.024		
		Dizygotic		
4 A	♀	0.074	0.036	
B		0.110		
5 A	♀	0.035	0.017	
B		0.052		
6 A	♀	0.144	0.060	
B		0.084		0.058
7 A	♀	0.205	0.174	
B		0.379		
8 A	♂	0.025	0.004	
B		0.029		
Intrapair variance ratio, dizygotics/monozygotics				11.7*

* Significant beyond the 0.05 level.