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and Barbara J. Krueckel

August 11, 1954

Berkeley, California

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August 11, 1954

ABSTRACT

A close relationship between the concentration of cholinesterase in the cerebral cortex of the rat and his adjustive-behavior patterns has been shown. The visual cortex, physiologically and cytoarchitectonically different from the other areas, is demonstrated to be different in cholinesterase concentration as well. Animals separated by a purely behavior test of hypothesis-preference show decided differences in the cholinesterase activity of the cerebral cortex.

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* We wish to thank Professor Melvin Calvin for his encouragement and cooperation in the conduct of this experiment. This work was in part supported by the U. S. Atomic Energy Commission.

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This is a preliminary report of a close relationship between concentrations of an enzyme in the cerebral cortex of the rat and his adjustive behavior-patterns.

In relating chemical events in the brain to behavior, it is desirable that both the chemical and behavioral tests meet certain requirements. Both should yield reliably quantifiable measurements of stable characteristics; both tests should permit the display of individual differences among the experimental subjects; and the chemical events and the behavior should have clear functional significance in the economy of the organism.

For our behavior test we used a standardized insoluble maze. The rat cannot learn the maze, since after each run the pattern of illumination cues and of correct alleys is changed. In his attempts to reach the food box the rat displays "hypotheses." Thus, for example, an animal may systematically choose the lighted alleys (a "visual hypothesis") or he may consistently choose the left alleys (a "spatial hypothesis") (1).

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This hypothesis behavior appears to meet all the requirements listed above as well as having additional advantages: 1. In five days of testing the rat makes 240 choices, and the strength of his hypotheses can be reliably quantified. 2. Rats tested in this apparatus show either visual or spatial hypothesis-preferences and large individual differences in the strengths of these preferences (1). 3. These preferences are stable over time (2) and are genetically determined (3). 4. The display of this behavior requires a minimum of physiological intervention by the experimenter. 5. The behavior is significant in the organism's normal adjustments insofar as it reflects his perceptual selectivity -- a selectivity which must occur if he is to organize the welter of diverse stimuli impinging upon him. 6. Finally, hypothesis-preference can be altered predictably by ablations in the visual and somesthetic areas of the cortex (2), thus suggesting the most profitable loci for chemical analysis.

Our chemical test measured the concentration of cholinesterase (ChE) in six areas of the cortex. In each hemisphere 10-20 mg. of tissue was taken from the visual, somesthetic and motor areas (the latter area for control purposes). The samples of tissue were weighed and homogenized in cold 0.9% saline and diluted to 10 ml. Eight to twelve mg. of tissue was used in each determination. The rate of hydrolysis of acetylcholine perchlorate (ACh) at pH 7.95 and 37° was determined anaerobically with a pH meter equipped to maintain constant pH through an automatic-recording syringe buret (4). Corrections were made for the "blank" hydrolysis of ACh (5).

Sixty male animals were tested behaviorally. Cholinesterase analyses

were made of the brains of ten rats with strong spatial preferences (Group I) and of ten rats with strong visual preferences (Group II). After behavioral testing, the animals were delivered, with neutral code designations, for chemical testing. They were decapitated and the samples of tissue were removed by gross dissection. The brains were preserved for exact determination of the sites of ablations.

The data are presented in Table 1. (The values for animal B-3, the first of our experimental animals to be tested chemically, deviates so widely--approximately four standard deviations--from the means of the rest of its group, that we have not used his data in the computations that follow. This animal's data are presented in the table in parentheses but will not be considered further in this paper.) The most general result is that the ChE activity of the rat's visual cortex is approximately 20% lower than that of either the somesthetic or the motor area. The respective t values are 3.83 and 5.92; thus, the probability of obtaining such differences by chance is approximately 1 in 1000. The visual cortex, physiologically and cytoarchitectonically different from the other areas, is demonstrated to be different in ChE concentration as well.

Perhaps even more interesting are the enzymatic differences observed when the animals are separated into two groups by the behavioral test. In the first place, the patterns of ChE activity are different. The visual-hypothesis rats show a progressive increase in ChE activity from the visual, through the somesthetic, to the motor area--the differences being statistically significant. The spatial animals show no consistent difference between the somesthetic and motor areas. Even more striking

are the differences in level of ChE activity. Group I shows significantly higher ChE activity than Group II in both sensory areas--the visual and somesthetic, but the groups do not differ significantly in the control motor area. The greatest differences is found when the ChE activities in the two sensory areas are averaged, $(V + S)/2$. All nine of the spatial animals score above 57.1 (the mean for all nineteen animals) and eight of the ten visual animals score below 57.1.

At present we would entertain two kinds of theoretical explanations to account for our data. The first would relate hypothesis-preference to ChE dominance of one of the sensory areas. Thus, for the spatial animals the S-V scores tend to exceed those of the visual animals. While this does not appear in the group averages (due primarily to animal Y-74), the trend is pronounced when individual animals are considered. The second theory would posit a general "power" factor--high ChE activity in the sensory ("cognitive?") areas makes for a more generally adaptive animal (more "intelligent?"). This assumes that a more adaptive animal shows spatial preference in our test. While certain theoretical considerations support this assumption, further behavioral and chemical tests are obviously necessary. We have begun research designed to test both the sensory-area dominance theory and the general "power" theory. In any event, animals separated by the purely behavioral test of hypothesis-preference show decided differences in the ChE activity of the cerebral cortex.

Most of the animals were drawn from Tryon's (6) three strains--maze-bright animals, maze-dull animals, and a cross between the two

(labelled "B", "D" and "C" respectively in Table I). Behaviorally, the B's are spatial, the D's visual, and the C's are found in both groups. Chemically, the B's tend to be high on the $(V + S)/2$ measure, the D's low, and the C's show a range which overlaps those of the other two strains. These data, while scanty, suggest that ACh metabolism in the cortex may be genetically determined and that this, in turn, determines hypothesis-preference. We plan to investigate this possible genetic-chemical-behavioral relationship through a selective breeding experiment.

References

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2. I. Krechevsky, J. Comp. Psychol. 19, 425 (1935).
3. I. Krechevsky, J. Comp. Psychol. 16, 99 (1933).
4. We are indebted to Drs. J. B. Neilands and M. D. Cannon who kindly permitted us to use the automatic recording titrator. It may be purchased from International Instrument Company, Canyon, California.
5. This is similar to the method used by M. H. Aprison, P. Nathan and H. E. Himwich, Science, 119, 158 (1954).
6. R. C. Tryon, Univ. Calif. Publ. Psychol. 4, 71 (1929).

Table 1

Hypothesis-preference Scores and Cortical Cholinesterase Activity
in Ten Spatial Preference Rats and Ten Visual Preference Rats with
t-Tests for Differences Between the Groups

Group I - Spatial

Group II - Visual

Rat No.	Pref. Scores*	Cholinesterase Activity in Different Cortical Areas**				Rat No.	Pref. Scores*	Cholinesterase Activity in Different Cortical Areas**			
		V	S	M	$\frac{V + S}{2}$			V	S	M	$\frac{V + S}{2}$
B-1	+185	56	69	62	62	D-44	-250	41	66	76	54
B-7	+150	52	72	64	62	D-12	-173	47	57	64	52
C-1	+142	56	61	58	58	X-52	-165	40	46	49	43
C-17	+136	51	71	70	61	D-46	-162	52	78	80	65
(B-3)	(+121)	(27)	(47)	(46)	(37)	D-18	- 92	41	54	66	48
Y-74	+103	79	55	69	67	C-3	- 74	46	52	54	49
C-28	+ 69	55	64	65	60	C-10	- 58	48	53	59	50
B-9	+ 42	56	69	82	62	X-55	- 51	52	54	63	53
C-26	+ 36	56	68	73	62	X-51	- 49	45	54	61	50
C-9	+ 35	59	70	74	64	X-53	- 24	63	63	70	63
Means N = 9	99.8	57.8	66.6	68.6	62.0	Means N = 10	-109.8	47.5	57.7	64.2	52.7
Overall means (N=.19)								52.4	61.9	66.3	57.1
t for differences between groups.								2.96	2.54	1.12	3.92
P01	.02	.3	.001

* Plus values indicate spatial, minus values, visual preferences.
 ** Expressed as moles ACh 10^{-10} hydrolyzed/min./mg. of tissue.
 Data for the two hemispheres of each rat have been averaged.