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INDIVIDUALITY AS EXHIBITED BY INBRED ANIMALS; ITS IMPLICATIONS FOR HUMAN BEHAVIOR

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That individual animals within an experimental group may possess an extraordinarily high degree of individuality is indicated by the work of Wade Brown and associates at the Rockefeller Institute published in 1925 and 1926.[1, 2] It requires some reading between the lines to arrive at this conclusion, because data with respect to individual animals are not given.

Male adult rabbits, 645 in number, were sacrificed and dissected and the weights of 17 organs (Table 1) were obtained. These weights were adjusted to take into

TABLE 1

RANGE IN RELATIVE ORGAN WEIGHTS OF 645 RABBITS

Organ	Grams per Kilo of Net Body Weight Minimum	Maximum	High/Low
Gastrointestinal mass	70.4	452.0	6
Heart	1.95	4.42	2.3
Liver	23.2	117.0	5
Kidneys	3.45	17.28	5
Spleen	0.035	2.93	80
Thymus	0.248	3.315	13
Testicles	0.47	4.93	10
Brain	3.33	8.16	2.5
Thyroid	0.048	1.23	25
Parathyroid	0.001	0.022	22
Hypophysis	0.007	0.035	5
Suprarenals	0.080	0.572	7
Pineal	0.002	0.025	12
Popliteal lymph nodes	0.05	0.382	8
Axillary lymph nodes	0.019	0.24	13
Deep cervical lymph nodes	0.02	0.295	15
Mesenteric lymph nodes	0.67	6.91	10

account the fact that the rabbits were not all the same size, and were expressed in terms of the weight of the organ per kilogram of net body weight. The variations between organ weights as expressed in this way are given in Table 1, and it will be noted that the least variation (heart) is 2.3-fold, the greatest variation (spleen) is 80-fold and the average variation of organ size in this group of rabbits is over 14-fold! The median variation is 10-fold. Unless one is inclined to reject the supposition that internal physiology is determined in part by the sizes of the various organs, including endocrine glands, it seems inescapable that among these 645 rabbits a high degree of individuality—not only anatomical but also physiological and biochemical—must have existed.

It is true that these rabbits were not an inbred group, but they were "carefully selected stocks of well nourished animals" representing the breeds commonly used for experimental work. Any one (or more) of the animals could be used in experimental work, and simply designated "rabbit." This particular group of animals is of interest because the variations observed, as based on coefficients of variations, were close to those cited for human populations.[1]

A subsequent study by Rosahn and Casey[3] showed that within a group of six healthy rabbits, followed for two years, statistically significant interindividual differences were found with respect to (1) red cell counts, (2) hemoglobin per cent, (3) total white cell count as well as counts of (4) neutrophils, (5) basophils, (6) eosinophils, (7) lymphocytes, and (8) monocytes. The individual consistencies with respect to these parameters are probably the result of inborn differences, related to the organ weight differences found by Brown *et al.*

Over a period of years, individuality, particularly with respect to excretion patterns and voluntary alcohol consumption in choice experiments, has been observed in our laboratories even in highly inbred animals. Such individuality was substantial in the case of rats which resulted from brother-sister mating for as many as 101 generations.[4]

We have now observed other manifestations of a high degree of individuality in inbred animals. For example, in newly hatched chicks of the same strain we find that susceptibility to alcoholic intoxication as scored on the basis of the usual symptoms (staggering, inability to stand, loss of righting reflex, unresponsiveness to stimuli) may vary 10-fold in a group of as few as 12 chicks.[5, 6]

The voluntary consumption of alcohol (4%) by members of a similar group of chicks over a four-day period, during which the influence of their drinking from a fixed position was obviated, varied from 1.5 ml for the lightest drinker to 35.0 ml for the heaviest. This was a 23-fold range when the inbred chicks were all receiving exactly the same food. One chick while on such a choice experiment remained heavily intoxicated most of the time, while some of its mates consumed practically no alcohol and most of them were unaffected by the amounts consumed.

The effects of the administration of carefully weight-graded, sublethal amounts of alcohol on the appetite impairment of chicks was also studied. It was found that with daily administration some chicks' appetites remained unimpaired and they gained weight at a rapid rate for a week, while other chicks of the same inbred strain lost their appetites almost completely, failed to gain, and finally died of inanition at the end of the week period.

The fact that there was no apparent correlation between these three different responses to alcohol on the part of individual baby chicks leads one to suspect that different nervous tissues were being affected predominantly by the alcohol in each case. The results are in keeping with the fact that among these inbred chicks, too, there is substantial anatomical variation.

More recently we have observed in inbred rats a similar high degree of individuality with respect to their appetites for different types of foods. For studying this we have offered weanling rats a free choice of the following food items in separate containers: (1) dried lean meat, (2) butter, (3) sugar, (4) raw carrots, (5) salt mixture, (6) fortified yeast. In one experiment, 39 rats were given these choices over a period of 17 days and the consumption of each item recorded for each rat. The variation in dried lean meat consumption varied 4-fold among the group, the variation in carrot consumption and salt consumption was about the same, the butter consumption varied 7-fold, that of sugar 17-fold, and that of fortified yeast 46-fold. Each animal exhibited a highly distinctive pattern of choices.

Even more striking evidence of individuality is observed when individual rats are allowed access to exercise wheels and records are kept of individual performance. In one experiment involving 10 inbred Sprague-Dawley rats kept under identical conditions of temperature, nutrition, etc., one rat traveled an average of 158 feet per day while at the other extreme one rat traveled an average of 9,500 feet per day (1.8 miles). The other eight rats exhibited a wide spread of intermediate values. It would appear that each individual rat has inborn tendencies which are determining factors in its eating, drinking, and exercise behavior.

Observations such as these are highly objective and can be repeated at will in many areas and with many different species.

We have pondered over these objective facts for some time seeking a better understanding of their basis. The only conclusion we can arrive at is that this individuality probably goes back to anatomical variability such as Wade Brown and co-workers observed at the gross level and Rosahn and Casey noted at the microscopic level. Each animal must behave distinctively in many ways because its entire anatomy, including its endocrine glands, is highly distinctive.

Going back one step further, let us ask the question: How can such wide anatomical variability exist within an inbred strain?

We cannot here go into a detailed discussion of the genetic situation or of all the possible explanations, but it is possible to consider one highly suggestive question: What are the factors which determine, in the case of the developing rat or chick, the exact direction that differentiation will take with each cell multiplication? Or to consider one obvious aspect, what factors determine in each animal what the relative organ weights will be? The answer is: The pertinent factors are largely undetermined.

These considerations suggest that genetic mechanisms which lead to extreme differentiation, such as takes place in mammals, fowls, and other complex organisms, must involve important factors which are not present in the genetics of organisms which produce substantially the same type of cells indefinitely without differentiation.

It also seems to us highly probable that these differentiation-determining factors must include *extra*-chromosomal agents, because highly differentiated cells supposedly bear the same chromosomes and genes as the undifferentiated cells from which they arise. Nondifferentiating cells also pass the same chromosomes and genes on to their progeny. In view of the unknown nature of the factors which govern differentiation, it would seem reasonable to postulate, until evidence is obtained to the contrary, that extrachromosomal factors are operative.

These observations seem to lie at the crux of the question of how inbred animals can have such highly distinctive organ weight patterns. There can be little doubt, based upon biological observations of long standing, that *inheritance* is a tremendously important factor in determining the morphological characteristics of a particular mammal or fowl. There likewise seems no escape from the conclusion that chromosomes and genes *are involved.* In light of the phenomenon of differentiation, however, it is seriously proposed that extrachromosomal factors are crucially important in determining the relative organ weights in a particular fowl or mammal.

There is no known mechanism comparable to that operating with genes and chromosomes whereby equal amounts of numerous extrachromosomal elements—nucleoli, mitochondria, ribosomes, endoplastic reticulum, protamines, histones, obscure hormonal factors, etc.—are passed on to the daughter cells with each cell division. Indeed if everything in the cells were reduplicated faithfully, differentiation and organ formation could not occur. Hence it seems logical to look among the extrachromosomal factors, including those presently unrecognized, for the influences responsible for variation of organ weights in individual animals. These considerations do not rule out the influence of the physical environment, or the recognition that a specified environmental influence might produce entirely different results depending upon the internal structure which is influenced. On the basis of these interpretations extensive inbreeding by brother-sister mating for many generations could not be expected to produce a uniform stock even if mutations were excluded.

Our tentative conclusions are therefore that a high degree of inborn individuality—anatomical, physiological, and biochemical—exists as an objective fact even in inbred strains, and that the basis for these inborn differences is presently out of reach of classical genetics and can be understood only when the extrachromosomal or other factors involved in differentiation are elucidated.

These conclusions are of particular importance in the human realm. According to this line of reasoning, monozygotic twins would not have precisely the same inheritance, for while the chromosomes and genes might be identical (if mutation did not intervene), the extrachromosomal elements would not be distributed with perfect equality in the first two daughter cells. That this idea is tenable is borne out by the fact that monozygotic twins vary substantially in their anatomic resemblance to each other. This has been observed by W. H. Sheldon[7] and is in line with the extensive twin studies of Kallmann,[8] and with observed differences in the excretion patterns of identical twins made in our laboratory.[9] The extrachromosomal elements in the first two daughter cells may be only approximately the same.

The question of the identical or nonidentical inheritance in monozygotic twins is of trifling importance to society, however, compared with the implications of these concepts for human health and human behavior in general.

Abundant evidence is available that variation in organ weights in "normal" humans is substantial. Over 50 years ago it was found that healthy adult male livers varied 2.8-fold in weight, kidneys 3.7-fold, brains 1.6-fold, and hearts 3.3-fold when as few as 69 cases were included in the study.[10] More recent data bear out the idea that each individual has a highly distinctive pattern of organ weights (and activities) including the highly important endocrine glands.[11, 12] Not only this, but evidence also shows that hormone levels, enzyme levels, and other biochemical parameters are distinctive for each individual.

These differences are the basis for the development of the branch of science we have called "propetology,"[13] the study of inborn susceptibilities and resistances toward a broad spectrum of specific diseases. These leanings are inherent in every member of the human population and understanding them will make possible the prevention of disease.

These differences have tremendous behavioral implications. Our food-choice experiments with animals have some parallel with a very recent study[14] of the food choices of adolescent boys and girls in which it was observed that each one exhibits individuality in this regard and that 10 out of 28 youngsters deviated "in a substantial way from the group average."

Earlier the author[15] described an experiment which led to the conclusion that each individual has a highly distinctive set of likes and dislikes in relation to all sorts of activities including those which may be regarded as the most important "reasons for living." These patterns of fundamental likes and dislikes are found in young and old alike and must show a considerable degree of durability. Presumably these variations are not only the result of environmental differences and culture but are in part a reflection of inborn anatomical (including endocrinological) differences.

One area in the behavioral realm which presents unusually poignant problems is that concerned with delinquency and crime. Sheldon and Eleanor Glueck of Harvard have been prominent students in this field for many years and their extensive observations have indicated that the onset of delinquent behavior occurs at 7 years or less in 44.4 per cent of delinquents and at 10 years or less in 87.6 per cent.[16] Also they find persuasive evidence of correlations between major physique types and tendencies to delinquent expression, through the intermediary of various physiological, neurological, and psychological traits which seemingly enhance the delinquency potential of the different body builds.[17]

Of course there is truth in the point insisted upon by the sociologists that crime can be fostered by bad living conditions and by bad associations. What is needed, however, is a far more complete picture. This includes the recognition that human individuals are by no means assembly line products and that the same environmental influences do not produce the same effects in all. Some youngsters are apt pupils, for complex reasons, when it comes to learning the arts of delinquency and crime; others under similar environmental conditions have stronger leanings toward conformity and good citizenship. A pathetic aspect of this problem resides in the probability that the very youngsters who become delinquent are potentially among the most valuable citizens. They will never rise to this estate, however, as long as the fundamental facts of biology are ignored, and environmental adjustments are made only on a statistical basis.

"Behavioral science," so designated initially by the Ford Foundation, has unfortunately tended to leave out a most important ingredient—biology.[18] Human biology needs at least ten times the attention it is now receiving from those who seek to understand human activities.[19]

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THE IDENTIFICATION OF THE RIBOSOMAL RNA CISTRON BY SEQUENCE COMPLEMENTARITY, II. SATURATION OF AND COMPETITIVE INTERACTION AT THE RNA CISTRON*

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The presence of a sequence in DNA complementary to homologous ribosomal RNA is indicated by experiments described in a preceding paper.[1] The data showed that a hybrid complex resistant to RNAase is formed when mixtures of ribosomal RNA and denatured DNA from the same cell are heated and then subjected to a slow cool.[2] When DNA from a heterologous source is substituted, no such complex is observed. The specific pairing of ribosomal RNA with a complementary sequence in DNA leads to the following two predictions: (1) The ratio of RNA to DNA in the specific complex should approach a maximum value at levels indicating the involvement of a minor fraction of the DNA; (2) Nonribosomal RNA should not compete for the same site.

Experiments relevant to these two issues have been performed. It is the intent of the present paper to describe the results obtained and discuss their implications. The data are consistent with the existence of a specific sequence in DNA capable of complexing with homologous ribosomal RNA and not occupiable by nonribosomal RNA from the same organism.

Materials and Methods.—Strain and preparation of materials: *E. coli* strains BB and A-155, a uracilless derivative of *B* were used in the present study. The methods of growth, labeling, counting, CsCl density gradient centrifugation, and the preparation of the following materials are detailed in the earlier papers;[1–3] heat-denatured DNA, free of RNAase; P^{32} and H^3-labeled 23S RNA free of "informational" RNA. The methods of assaying for RNAase activity and sensitivity of RNA-DNA complexes to nuclease degradation are the same as used in the earlier[1] study.

"Step-down" labeling of cells for informational RNA preparations: The procedure used is essentially that of Hayashi and Spiegelman.[3] Logarithmically growing *E. coli* A-155 cells in nutrient broth were collected by centrifugation, washed twice