

alteration in dosing procedure whereby our pregnant rats received far less meprobamate than did his own.

In order to eliminate any misunderstanding, we wish to emphasize that our pregnant rats received exactly the same amount of drug on exactly the same schedule as that described by Werboff, that is, 20 mg/kg per injection (three injections per day), or 60 mg per kg of body-weight per day for 4 consecutive days, a total of 240 mg of meprobamate per kg per rat. Therefore, our failure to reproduce his data cannot be due to any difference in drug doses or procedures used.

In the case of Hoffeld and Webster, who also used the same drug doses and procedures, Werboff attributes their failure to confirm his own report to two factors. Hoffeld and Webster's rats were pregnant at the time that they were shipped and probably suffered severe stress during this shipment. Secondly, the offspring of these rats were exposed to the stresses of colony housing and did not experience the handling and testing of the Werboff rats. But no explanation is offered as to why these rats should be healthier and learn better than Werboff's rats. Werboff's suggestion that the stresses listed above masked the deleterious effects of the drug is more puzzling than enlightening.

The fact remains that the results of Hoffeld and Webster agree completely with our findings. Both our group and theirs followed the procedures and schedules described by Dr. Werboff without difficulty, but failed to confirm his data.

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Threshold Regulation and Stimulus Wave-length

In a repeat of earlier research^{1,2} into the relationship between alpha abundance and visual thresholds for emotive words, red and green monochromatic lights were used as the visual stimuli. On the first presentation of each colour, results were in substantial agreement with those obtained in the previous work. Irrespective of stimulus wave-length, high thresholds for emotive words followed on sustained alpha abundance while low thresholds followed reduced alpha. The second presentation under a different colour, however, produced results which diverged somewhat from those previously reported. Irrespective of stimulus wave-length subjects tended to show higher thresholds for emotive than for neutral words, but those with higher thresholds for emotive words in red light showed reduced alpha abundance before reaching the threshold. This result is consistent with the finding^{3,4} that a red stimulus in juxtaposition to a potentially emotive subliminal stimulus will evoke emotional disturbance, and the finding⁵ that sympathetic activity decreases retinal sensitivity for light of long wave-length. All in all, the results suggest that while a given level of cortical activation may be necessary for awareness of a visual stimulus of low intensity, visual thresholds may also depend on a retinal variable under autonomic control.

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BIOLOGY

Allotypy and Eniotypy

INDIVIDUAL animals of a given species show well-defined, genetically controlled differences in the composition of certain isofunctional proteins. This molecular polymorphism is essentially of two types. The first type is one in which an isofunctional protein such as haemoglobin is present in all individuals of the species and the individuals differ from one another by the amino-acid sequence in limited regions of the molecule. The second type of polymorphism is characterized by the presence or absence of a particular protein in different animals of the same species. We wish to propose here a general nomenclature for these two polymorphic states.

Most instances of molecular polymorphism are of the first kind. When such polymorphism in the past has been revealed by the use of isologous antibodies, the phenomenon has been designated as allotypy (Oudin¹). We propose now to extend this term to include all kinds of polymorphism of the first type, irrespective of the method used to reveal it. Medawar² has recently made the same suggestion. For the second type of polymorphism we wish to propose the term 'eniotypy' (that is 'a type occurring in some', derived from the Greek ἐνί(σ)τε, 'somewhere'). One can distinguish between these two types of polymorphism by the hetero-specific reactivity of isologous antibody.

Isologous antibodies to a molecule with allotypic polymorphism show a very narrow range of cross-reactivity for, usually, they react only with molecules from animals of the same species as the immunized animal. As an example of this we may quote the failure of isologous antibodies to mouse or rabbit immunoglobulin to react with the sera of other mammals belonging to the same order. Isologous antibodies to a molecule with eniotypic polymorphism, on the other hand, would be expected to show a wide cross-reactivity with the corresponding isofunctional molecules from animals of other species, as was observed in the investigations of murine antibodies to the murine complement factor MuB1 (refs. 3 and 4).

Such experimental findings can readily be accounted for in terms of tolerance to autologous determinants^{3,5,6}, because the animal completely lacking a particular protein molecule will not be tolerant to any of its determinants. This lack of tolerance provides the animal with the capability of synthesizing antibodies against all the determinants on the injected molecule, including some that are shared by animals of different species and even different natural orders. As a result, a typical eniotypic antiserum, such as an antiserum to MuB1, reacts with the isofunctional proteins of a wide range of animal species and not just with proteins from other individuals within the species.

The foregoing classification of molecular polymorphism can be applied to an analysis of deficiency diseases such as various clotting defects (haemophilia, Christmas disease, absence of factors 5, 7, 8, and 10 (refs. 7 and 8) and metabolic deficiencies exemplified by total albinism (tyrosinase), Von Gierke's disease (glucose-6-phosphatase), familial goitrous cretinism (iodotyrosine deshalogenase), phenylketonuria (phenylalanine hydroxylase), Crigler-Najjar syndrome (glucuronyl-transferase)^{9,10} and acatalasaemia^{11,12}.

The inherited defects in these diseases may be due to a change in amino-acid composition (allotypy) which would affect the biological function of the molecule¹³, or might be attributable to a complete deletion of the synthesis of the molecule (eniotypy). In none of the instances enumerated here has it been definitively established whether the deficiencies are due to total failure to synthesize a biologically active molecule (eniotypy), loss of function resulting from amino-acid substitution of the functionally