Brain monoamine metabolism in the mouse during the immediate post-partum period

PAMELA M. GREENGRASS and SALLY R. TONGE* (introduced by B. E. LEONARD)

School of Pharmacy, Liverpool Polytechnic, Byrom Street, Liverpool L3 3AF

A number of studies have shown changes in hypothalamic monoamine concentrations during the oestrous cycle in rodents (Stefano & Donoso, 1967; Donoso, Stefano, Biscardi & Cukier, 1967; Bhargava & Gupta, 1966; Lichtensteiger, 1969). Changes also occur in other areas of the brain (Greengrass & Tonge, 1971; 1972). These latter changes may be related to the behavioural aspects of oestrus rather than to the control of ovulation; it is possible to abolish the active 'enticement reaction' without affecting other aspects of heat by removing small areas of the cortex (Beach, 1967) and to facilitate or inhibit hormone-activated oestrous behaviour in ovariectomized animals with drugs which alter monoamine concentrations (Meyerson, 1964). These observations suggest a role for sex hormone mediated changes in monoamine metabolism in the control of instinctive emotional behaviour. Disturbances of monoamine metabolism in the central nervous system are suggested to be involved in the aetiology of the affective disorders (Coppen, 1967), and the relatively high incidence of this type of mental disease at times when hormone levels are fluctuating widely may suggest a relationship between the female sex hormones and the psychological state.

We have studied monoamine metabolism in the mouse brain during the immediate post-partum period, when psychotic depressions frequently occur in the human female (Paffenberger, 1961). The concentrations of noradrenaline and 5-hydroxytryptamine, their precursors and metabolites, and the rates at which they disappear from the brain after synthesis blockade have been examined in the 'fore-brain' (cortex), the 'middle-brain' (thalamus, hypothalamus and striatum) and the 'hind-brain' (corpora quadrigemina, pons, medulla and cerebellum) and compared with similar determinations at dioestrus, when sex hormone activity is minimal.

Noradrenaline and dopamine concentrations in the fore- and middle-brain areas are significantly lower during the five days following parturition than at dioestrus. Normetanephrine concentrations, particularly in the middle-brain, are significantly elevated, suggesting an increased release of noradrenaline. The concentrations of both 5-hydroxytryptamine and 5-hydroxyindoleacetic acid are significantly lower than those found at dioestrus, whilst tryptophan concentrations are slightly elevated and this may suggest a decreased synthesis and release of 5-hydroxytryptamine. The rates of depletion of 5-hydroxytryptamine and noradrenaline after p-chlorophenylalanine and alpha-methyl-*p*-tyrosine respectively also suggest that the release of the monoamines is altered during the post-partum period. Some of these changes may be associated with the onset of lactation.

If the psychological state is controlled by the balance between tryptaminergic and noradrenergic activity in the central nervous system, then changes in the metabolism of the monoamines may contribute to the production of psychotic depressions at this time.

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A theoretical model for antigen aerosol provoked anaphylactic reactions *in vivo*

R. HICKS

School of Studies in Pharmacology, University of Bradford

When an anaphylactic reaction is provoked in an actively sensitized guinea-pig by exposure to an aerosol of the antigen using the microshock method of Herxheimer (1952), it may be assumed that the antigen gains access via the bronchioles to three tissue compartments containing antibody. The anaphylactic reaction depends upon interactions between antigen molecules (AG) and sessile antibody molecules ($AB_{(s)}$) fixed on an effector organ, to form a complex with an effective configuration AgAb (King & Francis, 1966). If a series of microshock reactions is induced by repeated exposure to the aerosol, by definition each should have the same severity, and it is assumed that each is provoked by a constant concentration of complex (c). Each antigen dose is limited to that sufficient to interact with the antibody in each compartment, such that the constant concentration of complex is formed.

The reaction may be represented by the equation

$$Ag + Ab_{(s)} = Ag\,Ab_{(s)} \text{--------(1)}$$

If relative concentrations are represented by (a) for antigen, (b) for sessile antibody and (c) for complex, and if the completion of the reaction corresponds to an equilibrium

$$K = \frac{c}{(a-c)\,(b-c)} \text{---------(2)}$$

If a series of microshock reactions is provoked by exposures at constant intervals (e.g. 2 h) the required duration of exposure increases progressively, and thus the requisite antigen is increased. This indicates desensitization, and one explanation is that the antibody available for complex formation is progressively depleted.

From equation (2) an expression representing the concentration of antigen reacting in each stage of the series may be derived:

$$a_n = \frac{c}{K}\left(\frac{n}{(b-nc)} - \frac{(n-1)}{(b-c\,(n-1))} + K\right) \text{------(3)}$$

where n=the number of exposures. Values for (a), derived from theoretical con-