ABSTRACT

It has not previously been suggested that prolactin may be involved in mental illness. Yet virtually every drug used in psychiatry either stimulates or suppresses prolactin secretion (Fluckiger, 1972). Prolactin causes renal sodium, potassium and water retention (Horrobin, 1973). It is bound to cerebral tissue and alters hypothalamic activity (Turkington and Frantz, 1972; Clemens, Gallo, Whitmoyer and Sawyer, 1971). Prolactin levels up to 100 ng./ml. potentiate the responses of smooth muscle cells to noradrenaline, while higher levels inhibit the responses: preliminary studies suggest that nerve cells behave in a similar way (Manku, Nassar and Horrobin, 1973). Emotional stress, surgery and drugs such as phenothiazines, reserpine and methyldopa can elevate human plasma prolactin levels into the 50-200 ng./ml. range (Frantz, Kleinberg and Noel, 1972; Friesen, Belanger, Guyda and Hwang, 1972).

Prolactin secretion is controlled by the hypothalamus which secretes prolactin-inhibiting factor (PIF), TSH-releasing hormone (TRH) and possibly prolactin-releasing factor (PRF). TRH is as effective in stimulating prolactin as TSH secretion (Bowers, Friesen and Folkers, 1972).

TRH has a rapid effect on mood in some depressed patients (Kastin, Ehrensing, Schalch and Anderson, 1972). Prolactin injected into humans may produce lethargy and irritability (Horrobin, 1973). Because of these observations and because of the effects of psychotropic drugs on prolactin secretion, I believe that prolactin and the hypothalamic factors which regulate its secretion may play key roles in mental illness. The main suggestions are:

1. Prolactin may be responsible for the neurotic behaviour which may be seen during periods of stress and in some women in the premenstrual period. Prolactin could account for the premenstrual changes in fluid and electrolyte balance (Horrobin, 1973).

2. Depression may be associated with elevated prolactin secretion and low levels of hypothalamic PIF, PRF and TRH. Prolactin is unusual among the anterior pituitary hormones in that its secretion rises when deprived of hypothalamic influences. Reserpine and methyldopa, which may both cause depression, both deplete the hypothalamus of PIF and elevate prolactin secretion.

3. Mania may be associated with low levels of PIF and high levels of either PRF or TRH, with consequent very high levels of prolactin. Mania and depression would thus be bipolar with respect to PRF or TRH but monopolar with respect to prolactin. The hypothesis could thus resolve the conflict between monopolar and bipolar models of mania and depression.

4. Schizophrenia may be associated with high levels of PIF and low prolactin secretion. This is compatible with the effectiveness of phenothiazines, which deplete PIF and elevate prolactin levels.

The hypothesis has been presented in bare outline. It is not necessarily inconsistent with the various amine hypotheses, since the amines exert at least part of their psychological effect by controlling secretion of hypothalamic factors. The main virtue of the hypothesis is that it is testable in humans, using established methods. I admit that it is unlikely to be true, but, as Popper has explained, provided that a hypothesis is testable, improbability is a virtue. When an improbable hypothesis turns out to be true the advance is much greater than when a probable hypothesis is proven.

Plasma prolactin levels can be accurately measured in human plasma by means of radioimmunoassay. The response of prolactin secretion to test injections of chlorpromazine can be used to obtain an indication of the rate of hypothalamic PIF secretion. In the presence of high levels of PIF the secretory response to chlorpromazine which depletes PIF is exaggerated. When PIF is depleted the response to chlorpromazine is depressed (Friesen, Hwang, Guyda, Tolis, Tyson and Myers, 1972). If the hypothesis is correct the following findings would be expected in the major psychoses:

1. Depression. Moderately elevated plasma prolactin levels with a depressed response to chlorpromazine.

2. Mania. Very high plasma prolactin levels, with a response to chlorpromazine similar to that in depression.


* There is an abundance of supporting data, which have had to be omitted here, but are available on request.
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References


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