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EDITORIAL

Studying brain receptor function: a neuroendocrine approach

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Abstract

A significant component of psychiatric practice relates to the management of patients with behavioural disturbance whose aetiology lies in the subtle alteration of brain biochemistry. The major handicap in assessing such patients, both from a clinical and a research point of view has been a lack of suitably sophisticated technology for studying brain function. Despite significant improvements in imaging technique and the development of positron emission tomography we are still lacking tools which assess brain receptor functioning. The neuroendocrine axis provides us with the means of assessing specific neurotransmitters in a safe and relatively inexpensive way. Such an approach is now widely used in research and has considerable potential within a clinical setting.

The fact that classic monoamine neurotransmitters are implicated both in affective disorders and schizophrenia and at the same time control hypothalmic-anterior pituitary function provides the basis for many psychoneuroendocrine investigations. The stimulation of certain central neurotransmitter systems results in the elevation of anterior pituitary hormones. If a pharmacologically selective drug is used, the rise in the anterior pituitary hormone gives some index of the integrity of the neurotransmitter pathway and the sensitivity of its receptor system. This approach is heavily dependent on the development of selective drugs for challenging specific receptor systems. As there are a myriad of potential confounding variables it is essential that there be rigorous control over such factors as gender, age, psychotropic drug exposure, weight loss etc.

The release of growth hormone (GH) from the anterior pituitary is under the control of 2 peptides, namely growth hormone releasing hormone (GHRH) and somatostatin (SS). Noradrenaline acting via the GHRH containing neurones stimulates the release of GH *(1,2)*. We now know that the stimulated release of GH through this mechanism is significantly blunted in patients with major depression *(3,4,5)*. When sone suppression and noradrenergic mediated GH release are both investigated in depressed patients, those subjects who show dexamethasone non-suppression are more likely to demonstrate blunted GH release than those with normal dexamethasone responses *(5)*. Acetylcholine (ACh) stimulates growth hormone release via the SS method *(6)*. It is now clear that depressed patients show enhanced release when their cholinergic system is challenged with pyridostigmine *(7)*. Overall therefore, depressed patients seem to have a down-regulation or under activity of their NA receptors and an up-regulation or over-activity of their ACh receptors.

GH release is also under GABAergic control. In a study of patients with major depression baclofen the GABA-B agonist was used to induce GH release. Baclofen (20 mg) significantly elevated GH levels in all healthy subjects but a blunting of response was seen in those patients with major depressive illness. The finding indicates diminished responsivity of the GABA-B receptor system in depression *(7a)*.

The release of prolactin from the anterior pituitary is under the inhibitory control of dopamine (DA) which acts directly on the lactotrophs of the pituitary. The release of prolactin is stimulated by serotonin *(8,9)*. There is now unequivocal evidence to indicate that 5-HT mediated prolactin release is blunted in major depression *(10,11)*. Such blunting has been demonstrated with a wide variety of probe drugs including l-tryptophan and fenfluramine. The abnormality is however not entirely specific to depression as patients with obsessive compulsive disorder and sociopathic personality disorder also demonstrate such blunting even in the absence of mood disturbance *(12,13)*.

The first evidence to emerge that central DA receptors might in some way control GH release was demonstrated by the administration of l-dopa which led to an increase in GH levels *(14)*. GH responses to the DA agonist apomorphine have been reported to be greater in patients with first rank symptoms of schizophrenia, but to be blunted in those patients with significant egative symptoms such as emotional flattening and

social withdrawal *(15,16)*.

The very complex neurotransmitter control of such hormones as GH and prolactin provides a window to the biology of neuro-behavioural disturbance. As a tool psychoneuroendocrinology is of relevance not just to the researcher but to the practicing psychiatrist as well.

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