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Editors' Introduction

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The following papers mostly derive from a symposium held during the 8th World Congress of Psychiatry in Athens. The symposium concerned the roles of stress, serotonin and other transmitters in depression, and particular attention was paid to the tricyclic antidepressant tianeptine, a drug with effects on serotonin which are strikingly different from those of other tricyclics.

The literature on life-event stress as a precipitant of depression in vulnerable subjects goes back at least as far as Freud. Emerging evidence suggests that the illness may develop through central effects of substances secreted in abnormally large amounts as a result of hyperactivity of the hypothalamo–pituitary–adrenal system. It may be relevant that much evidence indicates that this system is activated by serotonin. However, substantial neuroendocrine and other data indicate that central serotonergic function is impaired in depression. That the latter defect can play a causal role in the illness is consistent with the fact that numerous antidepressant drugs are thought to increase serotonergic function. For example, serotonin reuptake inhibitors increase the availability of the transmitter to post-synaptic receptors. The crucial role of this increase in the antidepressant action of the drugs appears to be confirmed by reports that treatments which oppose their effect on serotonin also reverse their therapeutic action.

In these circumstances, the antidepressant properties of tianeptine appear paradoxical as, in sharp contrast to other tricyclic antidepressants, it does not inhibit the neuronal reuptake of serotonin but enhances it, and thus decreases the availability of the transmitter to receptors. This finding both challenges prevailing concepts on the involvement of serotonin in depression and indicates new therapeutic avenues. It may also lead to improved understanding of mechanisms mediating the illness and its treatment. How tianeptine acts is unknown. One possibility is that it attenuates a serotonin-dependent activation of the hypothalamo–pituitary–adrenal axis. Another is that both tianeptine and conventional tricyclics, despite their opposite effects on neuronal uptake, may have a common effect on a critical balance of serotonergic responses. It is also conceivable that the antidepressant effect of tianeptine depends primarily on an interaction not with serotonin but with other transmitters, for example the catecholamines, as much evidence suggests that they also have important roles in depression and in mechanisms of antidepressant drug action.

Intriguing problems are raised, not only by the evidence that tianeptine has antidepressant properties but also by other indications that its profile of effects differs from those of other drugs which decrease the concentration of serotonin at receptor sites. The advent of this novel drug thus provides both a new therapeutic tool and a new stimulus for research on the role of serotonin and other transmitters in the brain.