

# Antidepressants

How effective are the new drugs in the elderly?

Dr Spiliou Argyropoulos and Professor David Nutt discuss the mode of action of the newer antidepressants and consider their role in the management of older people with depression

The pharmacological treatment of depression has been a success for psychopharmacology. Between 40 and 50 per cent of sufferers show complete recovery, with a further 25 per cent showing significant improvement—and these figures compare favourably with the outcome of chemical or surgical procedures in general medicine'. But how do antidepressants work to produce benefit? And are antidepressants effective in older depressed patients?

## Mode of action

The discovery of chemical treatments for depression was serendipitous. In the 1950s, imipramine (Tofranil) was initially tried in schizophrenia before it was observed that it had antidepressant properties, a discovery that led to the development of the tricyclics (TCAs). At the same time it was observed that iproniazid, used in the treatment of tuberculosis, had a positive effect on mood and, as a result, the monoamine oxidase inhibitors (MAOIs) were developed.

It soon became apparent that the net effect of the TCAs and MAOIs is to increase the availability of the monoamine transmitters, noradrenaline (NA) and serotonin (5HT) in the synapse. This led to the development of the monoamine hypothesis of depression (for example Schildkraut, 1965<sup>1</sup>), which postulates that a decrease of the available transmitters in the synapse is fundamental to the process of the illness and that antidepressants work by redressing this dysfunctional state.

## Key points

- The pharmacological treatment of depression has been a success for psychopharmacology with efficacy comparing favourably with the outcome of chemical or surgical procedures in general medicine
- The monoamine hypothesis still appears to be the most plausible explanation for the mode of action of antidepressants
- Sensitivity to drugs varies between older individuals, and the clinician should therefore not be dogmatic when prescribing to an elderly depressed patient, but should be alert to individual patient differences
- Newer antidepressants are probably a step forward in the treatment of depression in old age, although data on long-term efficacy are still required

But is the availability of NA and/or 5HT sufficient to explain the antidepressant effect of these drugs? In a series of elegant experiments, Delgado *et al*<sup>2</sup> showed that, if the brain is deprived of tryptophan (the natural substrate for the synthesis of 5HT), patients successfully treated with selective serotonin reuptake inhibitors (SSRIs) become depressed again. Similarly, if the production of NA is inhibited, patients treated with agents that specifically block the re-uptake of NA become acutely depressed<sup>3</sup>. It therefore appears that the monoamines are indeed needed for antidepressants to produce their effect.