published in Reader's Digest,
04 June 2015

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Antidepressants have been a staple in mental health care since their introduction in the 1950s. But how do they work and how far have they come since those early days?

The discovery of antidepressants

Some very serendipitous events happened in the world of drug discovery in the 1950s. Scientists found that drugs being studied to treat schizophrenia and tuberculosis showed antidepressant properties.

Closer examination revealed that both drugs increased levels of brain chemicals called monoamines (including serotonin and noradrenaline), and the ‘first generation’ of antidepressant drugs known as ‘tricyclic antidepressants’ (TCAs) and monoamine oxidase inhibitors (MAOIs) were born.

They are still in use today, though TCAs are used with caution due to severe side effects such as memory problems, blurred vision and even suicide in overdose; interestingly they are proving more useful in lower doses to treat chronic pain (for example, amitriptyline). MAOIs are still used but difficult to take because of possible severe drug and food reactions (especially cheese).

New… and improved?

Today, we are still benefiting from the earlier providence since all commercially available antidepressants still work by increasing levels of monoamines. The most widely prescribed are selective serotonin uptake inhibitors (SSRIs), including fluoxetine (prozac), citalopram (cipramil) and sertraline (lustral), and selective noradrenaline uptake inhibitors (SNRIs) including venlafaxine (effexor).

These drugs are safer than the earlier examples and really are effective in many cases, but side effects such as anxiety, nausea, loss of appetite and sleep disturbances exist. More worryingly, up to 50% of people don’t respond to treatment, and for those who do, effects are only seen after several weeks of treatment.

Even if they work, the British National Formulary recommends continuing taking the tablets for at least six further

months to reduce the risk of withdrawal. This has led some critics to question their usefulness: Dr Joanna Moncrieff of University College London noted that antidepressants show only a small advantage over placebo in some drug trials.

However, for all their negative publicity, real lives have been improved by antidepressants. Celebrities such as Brooke Shields and Sheryl Crow acknowledge the role that antidepressants played in their recovery, and countless other personal success stories exist.

The current lack of a gold standard antidepressant is probably because it is too simple to explain depression just in terms of a lack of monoamines in the brain. This is most strikingly demonstrated by the rapid antidepressant actions of ketamine (otherwise used as an illicit party drug or anaesthetic). It works on glutamate, an entirely different brain chemical. Scientists are even considering whether hormones such as oestrogen, thyroid hormone or stress hormones are involved.

The bigger picture

Beyond chemicals and hormones, depression results from complex emotional, psychological and social factors, so antidepressants are unlikely to be a total cure. Exercise, talking therapy and diet can all help. In many cases, ‘depression’ can be a natural reaction to life’s events.

Unhappiness is part of the human condition. However, when there are prolonged feelings of low mood, loss of interest or pleasure, sleeplessness, guilt or thoughts of suicide, antidepressant treatment should be considered, under careful review of a doctor. Left untreated, real torment with high socio-economic impact can result.

The World Health Organisation predicts that depression will be the leading global cause of disability by 2030.

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Links
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