

## Psychiatry in the doldrums: what price happiness?

Francis J Dunne

***A lifetime of happiness! No man alive could bear it: it would be hell on ear.*** (George Bernard Shaw 1856-1950)

Guess what? Antidepressants do not work for mild or moderate depression! This amazing 'revelation' seems to surface periodically as a popular item in the media and platform for the experts in living, especially since talking therapies are now considered the panacea for all ills. Despite methodological flaws in the research (as with all studies)<sup>1</sup> and noticeably, with less scrutiny of talking therapy research, this 'fact' is preferentially brought to our attention. That antidepressants have unpleasant side effects and are not always effective we have known all along. When one thinks about it, all drugs have adverse effects. Strange how antidepressants work - they seem to cause unpleasant adverse effects but not beneficial ones! No one doubts that neurotransmitters are involved in pain transmission or are responsible for muscle movement, yet biological pathways are dismissed when 'emotional' or 'psychological factors' are promoted as causing distress. By contrast, talking therapies cure the problem and are considered safe, it seems.

Am I alone in not being surprised? I have never understood how mild depression (whatever that is) becomes moderate, or how normal becomes mild, even with the International Classification of Diseases (ICD 10) and Diagnostic and Statistical Manual of Mental Disorders (DSM IV) to hand. And who has decided there be a minimum duration of two weeks for mild depression? Does it not count if one is suicidal for a week? The corollary of this is seen in another nugget of perceived wisdom masquerading as 'research' which informs us that 14 units and 21 units of alcohol per week are considered the upper limits of safe drinking for women and men, respectively. What if intake exceeds these magical figures? A rigid adherence to the dictum would castigate a woman or man as alcohol-dependent imbibing 15 and 22 units per week. This type of anecdotal research has no scientific meaning because one cannot equate units with a way of life, one's metabolism, stature, weight, and so forth. In the laboratory I can detect mild anaemia from severe anaemia because haemoglobin can be measured, and when to treat is usually quite clear-cut. In mental health studies, as with the alcohol example quoted, the theory is also vague. The usual response from 'researchers' in this field is that rating scales are capable of detecting differences in mood, say, which then determines the 'therapy' one receives. This is a fallacy. For

example, in medicine, small variations in haemoglobin do not make the slightest difference to how a patient feels, though such fluctuations are important.

How do you measure tiredness? One can feel tired and have a normal haemoglobin level. In the elderly, for example, abnormal blood indices are often present despite an outwardly well appearance. The anaemia still needs to be treated. Laboratory tests are therefore used to confirm the severity of an illness and are objective, regardless of outward appearances. Treatment is given and the haemoglobin (in this example) returns to normal, without the patient even being aware in many cases. The difference between the above example and a mental health 'condition' is that there is no realistic cut-off point between feeling well and being unwell. Therefore, when to intervene is arbitrary. Am I tired because I'm depressed, or is it the other way round? Do two or more weeks of mild happiness mean I am ill? 'Is there such a thing as moderate happiness?' 'Should we be using mood stabilizing medication or talking therapies if we are mildly or moderately happy?' Absurd. No one speaks of another individual as being mildly or moderately happy. So why should it make sense to talk of someone as mildly or moderately depressed? What next - mildly or moderately normal? Severe conditions require treatment; mild upsets can be managed by simple alterations in lifestyle, and one does not need a medical doctor or an expert in living to tell you so. There is little point in expecting a favourable drug treatment outcome for say, hypertension, if the patient continues to smoke or is grossly overweight. Take the metabolic syndrome of dyslipidaemia, central obesity, hypertension, and insulin resistance: treatment involves removing the causative factors, not prescribing drugs to reduce weight.

***I am a kind of paranoiac in reverse. I suspect people of plotting to make me happy.*** (J.D. Salinger 1919-2010)

The norm for most people is to get on with matters in hand and tolerate life's daily grind. Some good days, some bad. A lot depends on your financial status too. Nothing new there. It does not make sense to assume antidepressants will make the slightest difference to an individual's 'ups and downs,' as there is no clinical syndrome to address. Living is not a genetic condition, though alterations in genes affect living. There is the

risk of medicalising every difficulty one faces. Behaviour is often personality-driven and not a symptom of illness, and though personalities vary, one does not speak of a personality illness or personality condition. Even the term personality 'disorder' has come in for much criticism because of the difficulty in defining what is meant by personality.<sup>2</sup> One individual may be overtly aggressive, another too passive, and to embrace all eventualities, there is the term passive-aggressive. No point in being perfectionist because nowadays you may fit the obsessive character description. On reflection though, I would rather the cardiologist, surgeon, airline pilot, concert musician and so forth, err on the side of perfectionism! It does not require much imagination to realize that the real test of a 'condition' is when an individual begins to feel he/she is not functioning at a healthy level because of a pervasive sense of inertia, lassitude, lack of motivation, persistent gloominess and despair, for reasons apparent or not. Most people feel despondent at times, say after bereavement, or losing one's job, and likewise many individuals are more motivated, innovative, and ambitious than others. Some conditions, which seem to have a genetic basis, have stood the test of time, such as bipolar disorder, eating disorders, schizophrenia, borderline personality disorder and obsessive compulsive disorder; all other 'disorders' less so.

That antidepressants often fail to work is nothing new, even for severe depression because there are often too many factors at work. Patients who suffer from severe depression and suicidal ideation would be unlikely to be entering a clinical trial in any event. Furthermore, the theory of a chemical neurotransmitter imbalance is outmoded. It could be that an alteration in receptor sensitivity, either at the presynaptic or postsynaptic site, is the critical factor. Furthermore, it is conceivable that more neurotransmitters are involved than the handful we know of at present. What does the physician do then? Tell patients there is only a 70% chance of getting better with antidepressants and let them get on with it! Anyway, why should antidepressants be any different to other drugs used throughout the entire field of medicine? No drug has a 100% cure rate (save perhaps antibiotics or vaccines for specific infections). When one is well it is easy to be critical, cynical and dismissive. When a patient develops Hodgkin's Lymphoma or any other serious nonsurgical illness and is told there is a 70% chance of survival with medication it is highly likely he/she would optimistically choose the latter. Why should severe depression be any different?

Rating scales cannot be robustly be relied on, at least in psychiatry, as most information is descriptive and there are few instances when a scale can be regarded as having proven validity.<sup>3</sup> The Hamilton Rating Scale, a commonly used measure of depression, contains a large number of items relating to sleep and anxiety, and hence sedative antidepressants may seem to be appropriate. It could therefore be argued that the patient is benefiting from a good night's sleep rather than any inherent antidepressant effect of the drug in question. Thus the

side effect of the drug now has a therapeutic effect! This is akin to saying antihistamines work only through their sedative effect! Many scale items are poor contributors to the measurement of depression severity and others have poor interrater and retest reliability. Besides, mental and emotional diagnoses are so often ephemeral, and therefore defy 'rateability'. Another example is the Beck Depression Inventory (BDI), often used as a screening tool: because it is a self-report questionnaire, it poses problems in that the person completing it may distort responses. The question therefore is: how does one prove that antidepressants are effective on the basis of flawed clinical trials even when the evidence in clinical practice is obvious?

Meta-analysis is often used as 'proof' that research shows or does not show evidence to support a particular theory. However, meta-analysis itself is not foolproof. The methodology is complex and fraught with difficulty.<sup>4</sup> The sheer volume of material can impress the naïve and the search for negative outcomes, if it suits the preconceived, intended purpose, will be celebrated in the media as 'scientists discover' and so forth. A diligent search of the literature will uncover the sort of results one is looking for, because remember, there are lots of bad trials, no trials are identical, and there is heterogeneity among trial results.

It is clearly very difficult to devise a perfect rating scale, particularly in psychiatry where one is dealing in 'mind matters' and the pathoplasticity of mental disorders. Besides, leaving 'research' aside, the terminology in psychiatry as a whole is vague and interchanges between lay descriptions and 'psychiatric'. Does 'mad' mean psychotic? What is madness anyway? Is neurotic the same as being a worrier or chronically anxious? Can one be neurotic about one thing and not another? Is a teenager worried about exams (assuming he/she is fully prepared of course) normal, anxious, neurotic or unduly concerned? In medicine, matters are clearer by and large: blood pressure is high, low or normal. We are not comparing like with like, is the usual retort.

***To be stupid, selfish, and have good health are three requirements for happiness, though if stupidity is lacking, all is lost.*** (Gustave Flaubert 1821 - 1880)

Although it is easy to accept that antidepressants are ineffective for mild or moderate depression, one has to consider that in even in major depression the effects of spontaneous remission (75% in 12 weeks in some instances)<sup>5,6</sup> and natural fluctuations need to be taken into account. Even patients with chronic symptoms, who normally seek help when their symptoms are at their worst, sometimes improve anyway. Take a simple known fact: the prevalence of pain in patients with depression is high, around 65%, and the average prevalence of depression in pain clinics is nearly of a similar order. Pain symptoms in depression are not adequately treated by Selective Serotonin Reuptake Inhibitors (SSRIs) or indeed by amitriptyline (commonly used for pain relief) and hence depression is prolonged.<sup>7</sup> On

reflection it should not be too difficult to comprehend why drugs do not always work given that some three billion base pairs of deoxyribonucleic acid (DNA) make up the human genome. To add to the complexity, copy number variation refers to differences in the number of copies of a particular region in the genome, which is associated with susceptibility or resistance to disease.

Patients who are depressed and helped by medication are now being told by irresponsible 'counsellors' and sometimes by their own family doctors, that they are really only taking sugar pills, because of selective information taken from flawed antidepressant drug trials. By the same token should patients also give up their counselling sessions and take a sugar pill? It should not be forgotten that a true placebo control is impossible in psychotherapy unlike physical methods of treatment (though still difficult), whatever the flaws inherent in the latter. It seems odd that psychological data in 'therapy studies' carried out by non-clinicians and clinicians gets to be called 'science' whereas drug research carried out by scientists becomes 'flawed science?' Even so, countless dubious articles of 'human interest' manage to appear in prestigious medical journals under the apparent authorship of 'leading figures in the field' (being a pop celebrity physician or psychologist helps) where the psychobabble is fed to the reading classes who in turn regurgitate it to their naïve, well-intentioned adherents, and to the media. I don't blame the latter: all the media want is a good story; 'human interest' items will sell newspapers regardless of their quality or accurateness. People who run the media have little understanding of science and wear their ignorance as a badge of honour.<sup>8</sup> Therefore it comes as no surprise when it is discovered that antidepressants do not work for mild or moderate depression that the slogan becomes 'antidepressants do not work at all,' which is what the critical psychiatry faction wanted in the first place.

***If you can't explain it simply you don't understand it well enough*** (Albert Einstein 1879-1955)

Ironically, as in neuropharmacology, it is through progress in molecular biology that advances in psychotherapy research will be made as molecular genetic findings unfold over the next few years; it is likely that biological vulnerability will become increasingly detectable; although single genes and polymorphisms will probably never account for a large proportion of variability, combinations of genes may increasingly identify specific types of environmental vulnerability.<sup>9, 10</sup> No mental health condition is 'all genetic or environmental.' However, it is through neuropharmacological research that the mechanisms of action of various drugs used in neurology and psychiatry have been identified and helped to develop an understanding of biological substrates underlying the aetiology of psychiatric disorders. Genetic studies help us understand why some individuals are more prone to becoming ill given the same environmental stress factors.

The overriding clinical impression by doctors in clinical practice and in hospital settings is that patients tolerate minor side effects in the hope that benefits will accrue in the long term, as they do with the very unpleasant adverse effects from other drugs used in medicine (chemotherapy, for example). It is incumbent for doctors to stress that antidepressants do work for severe depression (though not in all cases) and mood stabilizers are helpful in bipolar disorder, and advise about untoward effects.<sup>11</sup> Doctors should also emphasize that the therapeutic effect is not that of a placebo, much in the same way that methylphenidate helps many children with Attention Deficit Hyperactivity Disorder (ADHD) when it is properly diagnosed and not attributed to poor parenting skills. The beneficial effects of antidepressants when they do occur are noticed objectively, usually within four to eight weeks of taking the medication, sometimes sooner. Patients are not coerced into feeling better by the charismatic charm of the physician, who may be sceptical to begin with, in any event. Besides, 'charisma' wears a bit thin when one continues to feel miserable and unresponsive to treatment of whatever sort. Cognitive therapy is effective for those who are motivated and not too disabled with lethargic indifference to engage. Behavioural methods do work, because specific techniques are employed which allow accurate objective evidence (cessation of smoking, desensitisation for phobias, amelioration of obsessive rituals) to be gathered.

There is a vast grey area between what constitutes 'normal' and 'mild or moderate' depression. In most cases, even if one concedes that a patient is 'mildly or moderately' depressed there is usually no need to interfere, because everyday issues are usually the triggering factors. Most 'psychiatric' conditions are not psychiatric, and life's ills and worries are best left to the General Practitioner (GP) to offer advice, perhaps a close friend, or even a next-door neighbour. Best to throw away all the psychobabble bibles and 'treatment packages' by the experts in living who earn a good income exploiting patients' weaknesses. Instead, patients should be taught to rely more on their natural intuition and cultivate inner strengths and talents. When depression, mood swings, phobias, obsessive rituals, and inner turmoil (for example, derogatory hallucinations, tormenting thoughts) become overwhelming, that is the time to seek medical advice. Most people (unless delusional) know which category they fit into, and should be able to receive help or intervention to deal with mental anguish before it becomes too disabling.

Many patients get better with or without talking therapies or medication, through sheer determination. At least with pharmacotherapy the medication can be thrown out after a reasonable period of adequate dosage. Either the drug works or it does not. Psychotherapy theoretically, particularly psychoanalysis, has no end, and can prove very costly. The top-up sessions are not free either! Even the National Health Service (NHS) will only offer a certain number of sessions and then you are on your own. Of course, there is the homework and perhaps

a few more top-up sessions, if you make enough fuss! By all means investigate the alleged fraudulent business practices of Big Pharma and eliminate the biased positive results of drug trials. Author bias should also be scrutinized to eliminate personal prejudice. There is no need for patients to be duped by the empty rhetoric perpetuated by the experts in living if we are simultaneously led to believe that life's ills will be resolved through the use of a sugar pill.

***To be conscious that you are ignorant is a great step to knowledge.*** (Benjamin Disraeli 1804 – 1881)

Within the field of psychiatry (and psychology) there are those who do not believe in drug treatments, ADHD, eating disorders, to mention a few. Everything is environmentally induced or caused by bad parenting, we are told by some self-appointed 'life experts'. And there are those who thrive on being deliberately controversial in an effort to raise their media profile and income. What a pity. Cardiology does not compete with cardiothoracic surgery nor does gynaecology compete with obstetrics, for example. Debate - yes. Antagonism - no. It is time for psychiatry to re-examine and distance itself from the popular psychobabble of the agony aunts and uncles before it completely loses its sense of professionalism. Because there are so many overlapping clinical scenarios within psychiatry and neurology, the former needs to align itself with the latter specialty and by doing so will gain respectability. The ever-widening chasm between psychiatry and other medical disciplines has been gathering momentum over the years, leaving psychiatry more alienated than ever. Perhaps there is also a case for subsuming some psychiatry specialties back into general psychiatry, for example, a Consultant General Psychiatrist with a 'special interest' in the conditions a Child Psychiatrist might be expected to deal with, such as Tourette's syndrome, ADHD, and psychoses. Fewer graduates are now interested in pursuing psychiatry because they do not want to

study medicine for years only to end up being marginalized as an on-looker in some multidisciplinary setting, devoid of any responsibility or decision-making. It is not that Cinderella will not be going to the Ball; there will be no Ball to go to.

#### Competing Interests

None declared

#### Author Details

FRANCIS J DUNNE, FRCPsych, Consultant Psychiatrist and Honorary Senior Lecturer, University College London, North East London Foundation Trust, United Kingdom.

CORRESPONDENCE: FRANCIS J DUNNE, FRCPsych, Consultant Psychiatrist and Honorary Senior Lecturer, University College London, North East London Foundation Trust, United Kingdom.

Email: francis.dunne@nelft.nhs.uk

#### REFERENCES

1. Ioannidis AP. Why most published research findings are false. *PloS Med.* 2010; 2(8): e124
2. Berrios GE. Personality disorders: a conceptual history. In: *Personality Disorder Reviewed*. Gaskell, 1993. Eds Tyrer P, Stein G Glasgow: Bell & Bain Limited.
3. Ferguson B, Tyrer P. Rating instruments in psychiatric research. In: *Research Methods in Psychiatry*. Gaskell, 1989. Eds Tyrer P, Freeman C. Oxford: Alden Press.
4. Eysenck HJ. Systematic reviews: meta-analysis and its problems. *Br Med J.* 1994; 309: 789.
5. Andrews G. Placebo response in depression: bane of research, boon to therapy. *Br J Psych.* 2001; 178: 192-194.
6. Zimbroff DL. Placebo response in antidepressant trials. *Br J Psych.* 2001; 178: 573-574.
7. Bair MJ, Robinson RL, Katon W, Kroenke K. Depression and pain co-morbidity: a literature review. *Archives of Internal Medicine.* 2003; 163: 2433-2445.
8. Goldacre B. *Bad Science*. London: Fourth Estate; 2008.
9. Fonagy P. Psychotherapy meets neuroscience: a more focused future for psychotherapy research. *The Psychiatrist.* 2004; 28: 357-359.
10. Plomin R, McGuffin P. Psychopathology in the postgenomic era. *Annual Review of Psychology.* 2003; 54: 205-228.
11. Dunne FJ. Lithium toxicity: the importance of clinical signs. *Br J Hosp Med.* 2010; 71: 216-210.