Depression and Medication

Dr Jonathan Haverkampf, M.D.

Depression comes in a multitude of flavors. Traditionally a distinction has been made between the reactive or neurotic depression on one end, which has been seen as largely environmentally induced, and the endogenic depression, which was largely seen as driven by biology. We now know that all three factors of biology, psychology and environment interact together in leading to the symptoms of depression.

The Circularity of Depression

Due to the plasticity of the brain, which regulates its morphological and chemical balance all the time, environmental influences can affect the circuitry and the functioning of the brain. Since the biology of the brain determines our thoughts and actions, it influences our environment, which again has a feedback on the brain. Thus, all effect depends on communication inside the brain and between the brain and the environment, and vice versa. This plays an immense role in the etiology and the symptoms of depression. It also explains why a combination of medication and psychotherapy in the majority of cases has the best outcome. Medication should be thought of in many cases of depression, except for the lighter reactive versions, while psychotherapy is always indicated if an individual suffers from depression. A condition that relies largely on communication deficits to be maintained, can also be cured through the 'talking cure', psychotherapy.

The Combination of Psychotherapy and Medication

Depression should in any case be treated with a combination of psychotherapy and medication if it is serious enough. Psychotherapy in most cases takes a few months to work, and medication, while also requiring a few weeks to work, will in many cases get results quicker than psychotherapy alone. In less severe cases, especially when it is a reaction to obvious external factors, psychotherapy alone may do. Medication can especially provide relief before the effect

of psychotherapy, which is more geared towards the long-run, takes hold. While medication cannot make life more meaningful per se, it can improve an individual's mood, which usually leads to more positive thoughts, a more positive outlook on the world, a decrease in ruminations, less anxiety and improved sleep – and appetite if that is desired.

Suicidal Ideation

Suicidality needs to be kept in mind in any form of depression and the mainstream opinion has shifted towards addressing these thoughts rather than avoiding talking about them out of fear that it might trigger them. Since the stability of the therapeutic relationship and communication itself are important tools in relieving depression, one should not be too anxious about naming issues that seem relevant.

A concern was that since the activating effect in several antidepressants can occur before the antidepressant affect, the risk for suicide might increase because a patient who still feels depressed becomes more active. However, the clinical experience is that the opportunity to talk about feelings and thoughts openly in a secure relationship reduces the urge towards self-harm.

Interests and Values

As I have outlined in another article on depression, facilitating the idea of a future the patient has some control over is often an important step in treating depression. This often means identifying values, interests and aspirations, which can provide greater motivation and a good feeling about the future, should be allowed enough space. There can be sadness about lost opportunities, but this usually subsides in the face of having a clearer direction in life and a greater promise of happiness, if one pursues the things one truly values and aspires to.

Medication

Unfortunately, the perfect medication does not exist. But this is also not to be expected since each antidepressant has a unique profile of effects, positive and negative, which can still be influenced largely by the unique biology of the patient. The following antidepressants are the most common ones. Using a single antidepressant (monotherapy) is usually to be preferred over polypharmacy. However, especially in more severe and treatment-resistant cases of depression,

combinations may have to be explored, such as combining venlafaxine and mirtazapine ("California rocket fuel") to yield an especially potent antidepressant and activating combination, which can even improve sleep (at lower to medium doses of mirtazapine).

Selective serotonin reuptake inhibitors (SSRIs)

The selective serotonin reuptake inhibitors (SSRIs) are the most common used antidepressants because of their relative safety and low side-effect profile. Unfortunately, in the beginning the indiscriminate use of the SSRI Prozac® against 'everything' from workplace problems to the stress of unhealthy living lead to a backlash in the media, which unfortunately made many patients avoid all medication out of fear to become emotionally flat or experience a change in one's personality, which has not been shown so far in any convincing way.

There are several other substances, that work as antidepressants, and all have potential side-effects. Often a substance is used which has a 'desirable' side-effect and that deals more effectively with the individual constellation of symptoms:

- Insomnia: Mirtazapine (Remeron® and many generics) is effective in inducing sleep at lower doses (around 15mg), an effect that seems to wear off once one goes up to 45mg. However, the antidepressant effect of 15mg is usually too small. Especially early on 'hangovers' in the morning are not uncommon. Among very common side effects are dry mouth, constipation, increased appetite, as well as somnolence, sedation, sleepiness (which may wear off).
- Lack of activation: Venlafaxine (Effexor®, Effexor XR®, Lanvexin®, Viepax®, Trevilor®) is a noradrenaline and serotonin reuptake inhibitor (NSRI) and often affectively increases activation. However, one should be careful with patients who might harm themselves (or others) because activation often occurs before the antidepressant effect takes hold. Also, if used in cases of anxiety it may increase the anxiety before reducing it.
- Co-morbidity with anxiety, panic attacks, OCD: the SSRIs are a good first choice. Venlafaxine seems to be helpful with anxiety, but often it increases anxiety early on, and possibly even medium-term.

Tricyclic antidepressants

Tricyclic antidepressants should not be used to treat symptoms that can be treated with the SSRIs or an NSRI, because of the letter's better safety profile. It is difficult to imagine there still is an application for MAO inhibitors, except in the rare depression that does not respond to

treatment. In the latter cases, my experience is that often medication has not been administered long enough or prescribed in the right dose. Quite frequently there has been no or only inadequate psychotherapy. It is worth remembering that psychotherapy is still and will always be the core treatment for what were a century ago referred to the 'neurotic' conditions, such as reactive depression, anxiety, OCD and the like. The reason is that the symptomatology can be traced to problems in interactions, communication and human relationships. Generally, there is better empirical evidence for the usefulness of antidepressants in the treatment of depression that is chronic (dysthymia) or severe.

In any case, it can take weeks for the full effect of medication to be noticed. A 2008 review of randomized controlled trials concluded that symptomatic improvement with SSRIs was greatest by the end of the first week of use, but that some improvement continued for at least 6 weeks.

Major depressive disorder

The UK National Institute for Health and Care Excellence (NICE) 2009 guidelines indicate that antidepressants should not be routinely used for the initial treatment of mild depression, because the risk-benefit ratio is poor. The guidelines recommend that antidepressant treatment should be considered for:

- People with a history of moderate or severe depression,
- Those with mild depression that has been present for a long period,
- As a second-line treatment for mild depression that persists after other interventions,
- As a first-line treatment for moderate or severe depression.

The guidelines further note that antidepressant treatment should be used in combination with psychosocial interventions in most cases, should be continued for at least 6 months to reduce the risk of relapse, and that SSRIs are typically better tolerated than other antidepressants.

Non-Responders

Between 30% and 50% of individuals treated with a given antidepressant do not show a response. In clinical studies, approximately one-third of patients achieve a full remission, one-third experience a response and one-third are non-responders. Partial remission is characterized by the presence of poorly defined residual symptoms. These symptoms typically include depressed mood, psychic anxiety, sleep disturbance, fatigue and diminished interest or pleasure.

It is currently unclear which factors predict partial remission. However, residual symptoms are powerful predictors of relapse, with relapse rates 3–6 times higher in patients with residual symptoms than in those who experience full remission.

"Trial and error" switching

The American Psychiatric Association 2000 Practice Guideline advises that where no response is achieved following six to eight weeks of treatment with an antidepressant, to switch to an antidepressant in the same class, then to a different class of antidepressant. A 2006 meta-analysis review found wide variation in the findings of prior studies; for patients who had failed to respond to an SSRI antidepressant, between 12% and 86% showed a response to a new drug. However, the more antidepressants an individual had already tried, the less likely they were to benefit from a new antidepressant trial. A later meta-analysis found no difference between switching to a new drug and staying on the old medication; although 34% of treatment resistant patients responded when switched to the new drug, 40% responded without being switched.

Combination

A combination strategy involves adding another antidepressant, usually from a different class of antidepressants to have effect on other mechanisms. Although this may be used in clinical practice, there is little evidence for the relative efficacy or adverse effects of this strategy.

Augmentation

For a partial response, the American Psychiatric Association guidelines suggest augmentation, or adding a drug from an altogether different class of substances. These include lithium and thyroid augmentation, dopamine agonists, sex steroids, NRIs, glucocorticoid-specific agents, or the newer anticonvulsants.

Which medication to use?

The medication used needs to be tailored specifically to the individual and the set of effects that are desired and those which need to be voided. However, there seem to be clear favorites overall, which the following list of antidepressant prescriptions in the US in 2010 shows:

Drug name	Commercial name	Drug class	Total prescriptions
Sertraline	Zoloft®	SSRI	33,409,838
Citalopram	Celexa®	SSRI	27,993,635
Fluoxetine	Prozac®	SSRI	24,473,994
Escitalopram	Lexapro®	SSRI	23,000,456
Trazodone	Desyrel®	SARI	18,786,495
Venlafaxine (all formulations)	Effexor (IR, ER, XR) ®	SNRI	16,110,606
Bupropion (all formulations)	Wellbutrin (IR, ER, SR, XL) ®	NDRI	15,792,653
Duloxetine	Cymbalta®	SNRI	14,591,949
Paroxetine	Paxil®	SSRI	12,979,366
Amitriptyline	Elavil®	TCA	12,611,254
Venlafaxine XR	Effexor XR®	SNRI	7,603,949
Bupropion XL	Wellbutrin XL®	NDRI	7,317,814
Mirtazapine	Remeron®	TeCA	6,308,288
Venlafaxine ER	Effexor XR®	SNRI	5,526,132
Bupropion SR	Wellbutrin SR®	NDRI	4,588,996
Desvenlafaxine	Pristiq®	SNRI	3,412,354
Nortriptyline	Sensoval®	TCA	3,210,476
Bupropion ER	Wellbutrin XL®	NDRI	3,132,327
Venlafaxine	Effexor	SNRI	2,980,525
Bupropion	Wellbutrin IR	NDRI	753,516

The Need for Psychotherapy

In any case, medication should always be combined with psychotherapy. In the less severe forms of depression and those that seem to have an explanation and are "reactive", medication often shows to be less effective and psychotherapy eventually leads in many cases to a full remission of the symptoms.

Dr Jonathan Haverkampf, M.D. MLA (Harvard) LL.M. trained in medicine, psychiatry and psychotherapy (psychoanalytic and CBT) and works in private practice for psychotherapy, counselling and psychiatric medication in Dublin, Ireland. The author can be reached by email at jonathanhaverkampf@gmail.com or on the websites www.jonathanhaverkampf.com and www.jonathanhaverkampf.ie.

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