OCD AND MEDICATION

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Psychotherapy is the first line of treatment when it comes to OCD. However, psychotherapy alone is often not enough, especially when a patient is so affected by the condition that leaving the home is no longer possible. Also, medication can be helpful in the beginning of therapy to reduce the level of anxiety and facilitate psychotherapy. It just needs to be pointed out that medication usually takes a significant while to work, frequently months, and in some cases even half a year to a year. One reason is that OCD is to a substantial part learned behavior which requires time to 'unlearn'.

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Introduction

Psychotherapy is the first line of treatment when it comes to Obsessive Compulsive Disorder (OCD). However, psychotherapy alone is often not enough, especially when a patient is so affected by the condition that leaving the home is no longer possible. Also, medication can be helpful in the beginning of therapy to reduce the level of anxiety and facilitate psychotherapy. It just needs to be pointed out that medication usually takes a significant while to work, frequently months, and in some cases even half a year to a year. One reason is that OCD is to a substantial part learned behavior which requires time to 'unlearn'.

If obsessive thoughts and/or compulsive behaviors interfere with life to an extent that its quality is noticeably reduced, then there is often a strong case for medication. Difficulties in relationships or at the workplace should be a clear signal that the OCD is no longer under control. They can also contribute to the underlying emotional conflicts that maintain the condition, and thus make it worse.

OCD

OCD affects people's life severely. It can make it impossible to leave the apartment, work and have a relationship. The patient focuses almost exclusively on thoughts and questions that cannot be resolved or answered. Often the thoughts are about issues that are unclear and uncertain, maybe about distant memories or ruminations or about another person's thoughts. The patient perceives a special relevance in them, which often seems out of proportion to an outside, which in psychotherapy can be addressed quite effectively by shifting the focus to his or her own wants, desire, wishes, aspirations and values. Quite often an emotional conflict between what patients feel they should do and what they want to do maintains the OCD.

There is significant evidence that certain areas in the brain and particular neurotransmitter systems, including serotonin and dopamine, are involved in the maintenance of OCD. Since the brain is a complex networked system where pathways interrelate and affect each other, it is difficult to say which neurotransmitter system and which morphological pathways are more primary in the chain of causation that ultimately leads to OCD. However, given the high plasticity of the nervous system and the enormous volumes of information that reach the brain, are processed by it and sent back out again, small variations in the network and in cellular functioning can lead to significant variations in such higher cognitive functions as recurrent thoughts and thoughts that induce other thoughts, in short, the thought patterns one uses and engages in.

Medication can support the autoregulatory mechanisms of the brain and lead to a reduction in obsessive thoughts and the urge to carry out compulsions, as well lessen the anxiety patients experience when they try to suppress their obsessive thoughts or compulsive behaviors. It is not exactly understood how this works but effects on both, the systems that make some people more predisposed towards OCD like thoughts and behaviors and those that mediate anxiety, seems plausible. In any case, the effects from medication are particularly slow in the case of OCD, often much more so than in the treatment of anxiety and depression, but if patients know this, thy are often more willing to accept the mostly mild and transient side effects that may occur in the first days or weeks.

SSRIs as First-Line Treatment

Effective medication is primarily from the class of selective serotonin reuptake inhibitors (SSRIs), which increase the intrasynaptic levels of the neurotransmitter serotonin and thereby change the density of various serotonin receptors in the cell membrane. The latter in conjunction with changes in the physiology and morphology of the neuro itself rather than the mere increase in the neurotransmitter seems responsible for the beneficial effect of this type of medication on depression, anxiety, OCD and other conditions. Most 'serotonergic' antidepressants have shown effectiveness in the treatment of OCD.

Paroxetine and Fluoxetine

Various studies have compared the effectiveness of SSRIs in randomized controlled trials (RCTs), but it seems that all SSRIs have a potential effect on OCD. However, there are some substances that are more likely to be used in daily practice than others. While fluoxetine (Prozac®) is used less often nowadays, mainly because it is more likely to cause feelings of numbness and the sense of being 'wrapped in cotton', and paroxetine (Paxil®) has been a stable and reliable candidate over the years, sertraline, and to some degree escitalopram, seem to be used increasingly. The problem with escitalopram is that it is licensed only in relatively moderate dose, and for OCD often higher doses are required.

Sertraline

Sertraline is effective for the treatment of OCD in adults and children. [1] It was better tolerated and, based on intention to treat analysis, performed better than the gold standard of OCD treatment clomipramine. [2] It is generally accepted that the sertraline dosages necessary for the effective treatment of OCD are higher than the usual dosage for depression. [3] The onset of action is also slower for OCD than for depression. [4]

Cognitive behavioral therapy alone was superior to sertraline in both adults and children; however, the best results were achieved using a combination of these treatments. [5][6]

From Anxiety to OCD

Selective serotonin reuptake inhibitors (SSRIs) seem to work because they reduce the anxiety that maintains the OCD and resurfaces if one tries to suppress intrusive thoughts or compulsive behaviors. SSRIs are usually tried first because they act predominantly on the serotonin system and have relatively safe side-effect profiles, but this does not mean that the effect is not also the result of pathways involving other neurotransmitter systems, as already mentioned.

Reducing anxiety with medication can make it easier for psychotherapeutic approaches, such as CBT or psychodynamic psychotherapy, to help the patient not to engage with the OCD thoughts and not to carry out the compulsive behaviors.

The Diversity of SSRIs

Generally, all SSRIs can have an effect of OCD, and it is often a matter of individual experience which one prefers. While at the turn of this century there was a preference for paroxetine, this might now be shifting to escitalopram, which is by many patients reported to be better tolerated, and often sertraline, which can be used at the necessary higher doses that escitalopram is not licensed for. Unfortunately, pharmaceutical companies lose interest to expand the indications of a drug, or its dose range, once the patents expired, as in the case of escitalopram. Clinical experience is crucial in any regard, because there are many different 'flavors' of OCD and co-morbidities which cannot be captured

adequately by most studies. A drug which is better in treating anxiety may be better in an individual suffering from both, OCD and anxiety, than one that causes activation and thus potentially more tension and nervousness.

The effect of the medication on the intracellular information transmission is likely responsible for the effect of SSRIs on the mentioned mental health conditions. The uneven distribution of receptor subtype in the brain and a host of other factors make the SSRIs quite specific. An increase in appetite associated with some SSRIs more than with others is likely due to the fact that the center in the brain communicating a hunger signal also uses serotonin as a neurotransmitter. In many patients this is an undesired side effect, while in some this may actually be of therapeutic value. A patient suffering from severe OCD and depression may have lost appetite to an extent that an SSRI which is more likely to increase his or her appetite may be desirable.

SSRIs that have been recommended repeatedly are the following:

- Citalopram (Cipramil®)
- Escitalopram (Cipralex®)
- Fluoxetine (Prozac®)
- Fluvaxamine (Luvox® and Faverin®)
- Paroxetine (Paxil® and Seroxat®)
- Sertraline (Lustral® and Zoloft®)

The NICE guidelines for the treatment of OCD now only recommend two of these medications for use in treating children with OCD. These are Sertraline for children aged 6 years and older and Fluvoxamine for children aged 8 years and older. However, there seems to be no theoretical reasons, why, for example, the newer and usually very well tolerated escitalopram should not also be useful in this regard.

Typically, the process of determining the most suited medication for an individual is achieved on a trial-and-error basis. However, to allow its maximum effects to be adequately observed, each medication should be taken for a specified time, usually for at least 12-16 weeks, before seeking out an alternative.

One should, of course, have an eye on potential side effects and contraindications to the SSRIs, such as a large QT prolongation or side effects from SSRIs in the past that did not fade after a few weeks. Any allergic reactions, such as rashes, on one SSRI occur again on a different SSRI.

High Doses

Relatively high doses of SRIs are needed for effectiveness in the treatment of OCD. [25] Studies have found that high dosages of SSRIs above the normally recommended maximums are significantly more effective in OCD treatment than lower dosages (e.g., 250 to 400 mg/day sertraline versus 200 mg/day sertraline). [25][28] There is a case report of complete remission from OCD for approximately one month following a massive overdose of fluoxetine, an SSRI with a uniquely long duration of action. [18]

Discontinuing SSRIs

Although SSRIs can be stopped quite easily, it is sensible to reduce them gradually. NICE recommend that if the medication has helped, one should continue taking the medication for at least 12 months to ensure your symptoms continue to improve. This makes it also more likely that there will be an often empirically observed protective after-effect after stopping them.

Non-selective serotonin reuptake inhibitors (NSSRIs)

If these medications fail to work, an NSSRI, mostly a tricyclic antidepressant, may be prescribed. However, because it affects a greater variety of neurotransmitters and receptors in the brain, the breadth of potential side is greater. Therefore, the NSSRIs are not first-choice medication for treating OCD.

Clomipramine

Clomipramine (Anafranil®) is a tricyclic antidepressant that has been used in the past and may be a secondary choice to the SSRIs. The NICE guidelines state Clomipramine should be considered in the treatment of adults with OCD or BDD after an adequate trial of at least one SSRI has been ineffective or poorly tolerated, or if the patient prefers Clomipramine or has had success in using the medication before.

Clomipramine was the first drug that was investigated for and found to be effective in the treatment of OCD. [50][22] In addition, it was the first drug to be approved by the FDA in the United States for the treatment of OCD. [8] The effectiveness of clomipramine in the treatment of OCD is far greater than that of other TCAs, which are comparatively weak SRIs; a meta-analysis found pre- versus post-treatment effect sizes of 1.55 for clomipramine relative to a range of 0.67 for imipramine and 0.11 for desipramine. [21] In contrast to other TCAs, studies have found that clomipramine and SSRIs have similar effectiveness in the treatment of OCD. [21] However, multiple meta-analyses have found that clomipramine nonetheless retains a significant effectiveness advantage relative to SSRIs. [13] However, the effectiveness advantage for clomipramine has not been apparent in head-to-head comparisons of clomipramine versus SSRIs for OCD, [13] which may also be a consequence of the different methodologies used.

The combination of clomipramine and SSRIs has also been found to be significantly more effective in alleviating OCD symptoms, and clomipramine is commonly used to augment SSRIs for this reason. [25][8]

In addition to serotonin reuptake inhibition, clomipramine is also a mild but clinically significant antagonist of the dopamine D1, D2, and D3 receptors at high concentrations.[13][32] Addition of antipsychotics, which are potent dopamine receptor antagonists, to SSRIs, has been found to

significantly augment their effectiveness in the treatment of OCD. [13][27] As such, besides strong serotonin reuptake inhibition, clomipramine at high doses might also block dopamine receptors to treat OCD symptoms, and this could additionally or alternatively be involved in its possible effectiveness advantage over SSRIs. [26][12]

Although clomipramine is similarly or more effective in the treatment of OCD compared to SSRIs, it is greatly inferior to them in terms of tolerability and safety due to its lack of selectivity for the SERT and promiscuous pharmacological activity. [13][10] In addition, clomipramine has high toxicity in overdose and can potentially result in death, whereas death rarely, if ever, occurs with overdose of SSRIs. [13][10] It is for these reasons that clomipramine, in spite of potentially superior effectiveness to SSRIs, is now rarely used as a first-line agent in the treatment of OCD, with SSRIs being used as first-line therapies instead and clomipramine generally being reserved for more severe cases. [10]

Augmentation with a neuroleptic

In very severe cases with intrusive thoughts one can also add a neuroleptic, whereby possible cross interactions should be kept in mind. Generally, one should avoid combinations that can increase the risk of the otherwise very rare serotonin syndrome, which can be life-threatening and requiring intensive care. Also, one needs to be careful with combinations that prolong the QT time. Olanzapine (Zyprexa®) may be the least problematic on the last point, but it also can prolong the QT time.

Psychotherapy

Medication should not be given alone. It should always be used together with psychotherapy, except in cases where this is not possible.

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