Drug treatment of obsessive-compulsive disorder

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Knowledge of pharmacotherapeutic treatment options in obsessive-compulsive disorder (OCD) has grown considerably over the past 40 years. Serotonergic antidepressants, such as selective serotonin reuptake inhibitors (SSRIs) and clomipramine, are the established pharmacologic first-line treatment of OCD. Medium to large dosages and acute treatment for at least 3 months are recommended until efficacy is assessed. In case of significant improvement, maintenance treatment is necessary. Unfortunately, about half of the patients do not respond sufficiently to oral serotonergic antidepressants; augmentation with atypical antipsychotics is an established second-line drug treatment strategy. Alternatives include intravenous serotonergic antidepressants and combination with or switch to cognitive behavioral psychotherapy. Remarkably, a considerable proportion of OCD patients still do not receive rational drug treatment. Novel research approaches, such as preliminary treatment studies with glutamatergic substances, and trials with further drugs, as well as needed aspects of future research, are reviewed.

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While only a few decades ago "obsessive neurosis" had been regarded as a psychiatric condition that was mostly treatment-refractory, several effective therapeutic strategies for obsessive-compulsive disorder (OCD)—both psychotherapeutic drugs and behavioral psychotherapeutic techniques—began to evolve during the last third of the 20th century.

In terms of modern pharmacotherapy, the first hints of the efficacy of clomipramine, a tricyclic antidepressant (TCA), which inhibits serotonin reuptake, date back about 40 years.[1-3] In the 1970s, research with more stringent designs in this area began, and soon placebo-controlled trials showed the antiobsessive and anticompulsive action of clomipramine.[4-6] Interestingly, specific anti-OCD effects were even observed when comorbid depression was rigorously excluded. Treatment of OCD patients may require relatively high doses for an extended period of time, which may be accounted for by a greater delay of effect in the orbitofrontal cortex, which is thought to be implicated in OCD.[7] A possible role of serotonergic neurotransmission in the pathophysiology of OCD was surmised by the results of the studies with clomipramine, by later numerous investigations showing the therapeutic action of different selective serotonin reuptake inhibitors (SSRIs) in OCD, and by additional findings, such as the provocation of OCD symptoms by the serotonergic agent m-chlorophenylpiperazine.[8-10] Interestingly, predominantly noradrenergic drugs, such as the TCAs desipramine[11] and nortriptyline[4] were less

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effective than clomipramine. The additional importance of dopamine[12,13] and glutamate dysfunction[14,15] in the pathophysiology of OCD has been established, and led to pharmacotherapeutic applications beyond serotonergic drugs.

Notwithstanding the progress of pharmacotherapy of OCD, even nowadays a high percentage of patients with OCD obviously do not receive adequate drug treatment: upon admission to a northwest European university psychiatric centre, more than one third never had received any pharmacotherapy, one in seven had received inappropriate drugs, and half of the patients had never been treated with an adequate dose of a serotonin reuptake inhibitor (SRI).[16] An interesting side aspect of pharmacotherapy of OCD is that patients with OCD show a considerably lower placebo response than subjects with other anxiety disorders, which is not caused by differential expectancy.[17] This phenomenon, and data about the rarity of spontaneous remission of OCD in all age groups,[18] add evidence for the necessity of administering effective therapeutic approaches to try to reduce long-term morbidity.

In this brief review, current pharmacotherapeutic treatment options for OCD in adults will be highlighted, beginning with established first-line treatments. Then, special emphasis will be given on worthwhile, but still preliminary, strategies for treatment-refractory patients. Finally, a short perspective of potential future aspects of pharmacotherapy of OCD will be discussed.

First-line agents in OCD: SSRIs and clomipramine

SSRIs and the SRI clomipramine are recommended as first-line agents for drug treatment of OCD due to the convincing database from numerous published randomized controlled trials (RCTs), according to several meta-analyses,[19] current expert guidelines, and consensus statements.[20-24] Rather than citing the ample single and mostly equivocal research papers, reference to some of the latter articles will primarily be given in this section.

The current guidelines of the World Federation of Societies of Biological Psychiatry (WFSBP) for the pharmacological treatment of OCD[24] grant the highest category of evidence ("A", ie, full evidence from several RCTs) for the SSRIs escitalopram, fluvoxamine, fluoxetine, paroxetine, and sertraline, as well as for the TCA clomipramine, but not for any other drug. Because clomipramine is less well tolerated than the SSRIs, it was given a recommendation grade of 2 (moderate risk benefit ratio), while the SSRIs received the highest recommendation grade 1 (good risk:benefit ratio). As for citalopram, only one positive double-blind, placebo-controlled study was published, and only a recommendation grade of 3 (limited evidence from controlled studies) was given.

This WFSBP guideline mentions that usually lower response rates are achieved in OCD in comparison with other anxiety disorders, and that sometimes only partial remission is achieved. As a rule, somewhat higher doses are used for these drugs in OCD than for other anxiety disorders, higher doses being associated with greater efficacy in some, but not all, evaluations. In several long-term and relapse-prevention studies, SRIs were shown to be superior to placebo, pointing to the requirement of long-term treatment of OCD. According to a systematic review on all long-term, placebo-controlled trials with SSRIs in OCD,[25] the likelihood of relapse during 24 to 52 weeks of treatment was significantly lower on an SSRI than with placebo. Thus, successful treatment with SSRIs should be maintained at the maximal effective dose for at least 12 months.

An extensive display of the many acute treatment studies on SSRIs versus placebo, different doses of SSRIs, SSRIs versus other SSRIs, clomipramine versus placebo, SSRIs versus clomipramine, SSRIs versus placebo, or clomipramine for continuation treatment and SSRIs vs placebo or clomipramine for relapse-prevention treatment can also be found in the guidelines on core interventions in the treatment of OCD of the National Institute for Health and Clinical Excellence (NICE) of the British Psychological Society and the Royal College of Psychiatrists.[21] According to these guidelines, the initial pharmacological treatment in adults with OCD should be one of the following SSRIs: fluoxetine, fluvoxamine, paroxetine, sertraline, or citalopram. Of note, studies on the efficacy of escitalopram in OCD were published only later.[26]

A current Cochrane review of placebo-controlled SSRI trials in OCD, comprising 17 studies with 3097 participants, also showed efficacy for all SSRIs included (citalopram, fluoxetine, fluvoxamine, paroxetine, and sertraline).[27] The authors detected no statistical differences in short-term therapeutic action among the individual SSRIs. For a reliable estimation of potential differences in tolerability between the different SSRIs, further study is needed.

Treatment of OCD patients refractory to serotonergic antidepressants

Despite the proven efficacy of SSRIs and clomipramine in OCD, as shown above, about 40% to 60% of patients show no or just partial symptom improvement to a treatment with a first-line drug.[28] Therefore, the search for effective second-line treatment strategies in drug-refractory OCD patients is of great clinical importance. However, most of the following options still stand on considerably weaker empirical grounds than the well-established first–line recommendations described above.

Modification of serotonergic drug therapy with first-line agents

Intravenous clomipramine was shown to be more effective than oral clomipramine in two double-blind placebo-controlled trials,[29,30] and thus was considered a recommendation grade 3 strategy for treatment-resistant OCD patients (limited evidence from controlled studies).[24] Regarding citalopram, an open trial showed a beneficial and relatively rapid response in OCD patients resistant to previous oral therapy.[31] However, more sophisticated studies are still needed.

High-dose treatment with serotonergic drugs is another strategy worth considering. Greater improvement with higher vs lower doses of SSRI was reported using 250 to400 mg/d vs 200 mg/d of sertraline[32] and with escitalopram after an increase of dose from 20 up to 50 mg/d.[33] However, two recent studies with escitalopram contradict the notion that a positive response requires higher doses of treatment. A similar response after 24 weeks of 10 mg/d vs 20 mg/d was shown in a double-blind placebo-controlled study.[26] In an open study, a superior reduction in OCD symptoms was found with 30 mg/d vs 20 mg/d of escitalopram, which, however, disappeared when initial comorbid depression and anxiety were considered as analysis covariates.[34]

Whether switching from one first-line drug to another may be advisable, is still an unresolved issue. In one open study, switching from one SSRI to another resulted in a lower response rate (0% to 20%) than switching from one SSRI to clomipramine (33% to 40%).[35] Although meta-analyses have reported a larger treatment effect of oral clomipramine than for SSRIs, head-to-head comparator studies do not support this evidence.[36]

Some open-label studies suggest that combined treatment of clomipramine and an SSRI is effective and well tolerated. Positive results have been reported with long-term augmentation with citalopram (up to 60 mg/d) in 20 treatment-resistent OCD patients on clomipramine.[37] In smaller samples, encouraging data have also been reported with the combination of clomipramine with fluoxetine[38] or with sertraline.[39]

Augmentation with antipsychotics

The combination of the antipsychotics risperidone, haloperidol, olanzapine, or quetiapine with an SSRI was shown to be more effective than SSRI monotherapy in treatment-resistant cases and is recommended (grade 3, ie, limited evidence from controlled studies) by the WFSBP guidelines.[24] In most studies, response occurred within 1 month of augmentation. After such treatment, which should be initiated only after at least 3 months of maximally tolerated therapy of an SSRI, about one third of treatment-refractory OCD patients show a clinically meaningful amelioration.

In several meta-analyses positive acute effects of antipsychotic augmentation were demonstrated.[40-42] Despite their recommendation, the WFSBP guideline[24] mentions that evidence for the efficacy of quetiapine and olanzapine was still inconclusive according to respective systematic review.[40] Further meta-analyses about quetiapine showed equivocal results.[43,44] A recent double-blind augmentation study with quetiapine in severe OCD patients failed to show an effect of quetiapine.[45] In contrast, superior effects of quetiapine versus ziprasidone as an adjunct to SSRI were found in treatment-resistant OCD patients in a retrospective study.[46] Interestingly, (primary!) addition of quetiapine to citalopram was more effective than citalopram alone in reducing OCD symptoms in a large double-blind study in treatment-naïve or medication-free OCD patients,[47] although extrapolation of these results to augmentation studies sensu stricto may be problematic. Regarding olanzapine, a single-blind study comparing risperidone versus olanzapine augmentation of SSRIs showed positive responses without differences between the two treatment groups.[48] The long-term effectiveness of atypical antipsychotics in the augmentation of SSRIs has so far not sufficiently been studied and was not supported in a trial using olanzapine, quetiapine, and risperidone.[49]

Several further atypical neuroleptics are promising new candidates for augmentation therapies of serotonin reuptake inhibitors according to various case reports and open studies. In a 12-week, open-label, flexible-dose trial of aripiprazole, significant improvement of OCD symptoms was demonstrated.[50] Some respective case reports with aripiprazole had been published before.[51] Even as monotherapy, a case series suggests that aripiprazole holds promise for treating OCD.[52] Also for amisulpride augmentation, an open study has shown promising results.[53] Augmentation with perospirone resulted in beneficial effects in a case report.[54]

Augmentation with or switch to cognitive-behavioral psychotherapy

Preliminary evidence supports the usefulness of cognitive-behavioral therapy (CBT) as a nonpharmacological augmentation treatment. In a randomized controlled trial in patients who were on a therapeutic dose of SSRI for at least 12 weeks, and continued to display clinically significant OCD symptoms, the augmentative effect of exposure and ritual prevention versus stress management training was compared; after 8 weeks significantly more patients with exposure and response prevention showed a decrease of symptom severity of at least 25% and achieved minimal symptoms.[55] In a naturalistic setting, the usefulness of CBT (including exposure and ritual prevention) in nonresponders to at least one adequate trial with a serotonergic antidepressant was shown, while pharmacologic treatment underwent no changes under the trial.[56] In patients responding to 3 months of drug treatment, but showing residual symptoms of OCD, a greater improvement of OCD symptoms after addition of behavior therapy for 6 months versus continuation of drug treatment alone was shown, and significantly more patients achieved remission.[57] However, no control condition for behavior therapy was used.

Also, a switch to CBT should be considered. In a wait-list-controlled open trial, patients with a history of an inadequate response to multiple serotonin reuptake medications in adequate doses were treated with 15 sessions of outpatient CBT, incorporating exposure and ritual prevention.[58] OCD symptoms decreased significantly and gains were maintained over 6 months. Further studies with more elaborate designs are needed. Although a meta-analysis of psychotherapy and pharmacotherapy for OCD[59] found highest effect sizes for combined treatment, no clear advantage for the combination of serotonergic antidepressants and CBT was detected in the individual controlled trials published so far.[60]

Augmentation with or switch to other drugs

Numerous further drugs have been studied for augmentation or in monotherapy for the treatment of OCD, but so far, none of these approaches described below has reached sufficient empirical evidence to become recommended in treatment guidelines.[24] However, some of these drugs seem promising for further study and may be attempted in OCD patients, who were refractory to treatments with superior current evidence.

Glutamatergic agents are among the most exciting new candidates in the treatment of OCD.[14,15] In an open-label augmentation trial with memantine, an N-methyl-D-aspartate (NMDA) glutamate receptor antagonist, a meaningful improvement of symptoms was seen in nearly half of the patients, who had failed to respond to treatment with an SSRI for at least 3 months.[61] Case reports of refractory OCD patients successfully treated with an augmentation of memantine were published previously.[62,63] Interestingly, adjunctive glycine (an NMDA glutamate receptor agonist) was also tested in a small double-blind placebo-controlled trial and approached efficacy for treatment of OCD symptoms.[64] For the glutamate-modulating agent riluzole, which was added to existing psychopharmacotherapy in treatment-resistant OCD patients, significant antiobsessional effects were observed in an open-label trial.[65] Also, amantadine (another NMDA antagonist) could be a useful drug for the treatment of OCD according to preclinical findings,[66] but human studies are so far missing. Augmentation with topiramate, among other actions an α-amino-3-hydroxyl-5-methyl-4-isoxazole-propionate (AMPA) glutamate receptor antagonist, in treatment-resistant OCD patients may be beneficial.[67,68] Respective double-blind studies with topiramate are on their way (ClinicalTrials.gov Identifiers: NCT00211744 and NCT00182520). Also for pregabalin, which can indirectly inhibit glutamate release via blockade of calcium channels, beneficial effects on OCD symptoms in combination with serotonergic antidepressants have been reported in case reports.[69,70] A double-blind placebo-controlled study with pregablin in SSRI-refractory OCD is being conducted (ClinicalTrials.gov Identifier: NCT00994786). For aug-

mentation of fluoxetine in a treatment refractory patient with glutamate modulator N-acetylcysteine, a marked decrease of OCD symptoms was observed.[71] A double-blind study with this agent is currently recruiting patients with OCD (ClinicalTrials.gov Identifier: NCT00539513). Another interesting development with a glutamatergic agent involves D-cycloserine, a partial agonist at the NMDA receptor, which was found to facilitate fear extinction learning in preclinical and human studies when administered before or shortly after exposure to fearful cues.[72] D-cycloserine augmentation of psychotherapy with exposure and response prevention in OCD has so far been investigated in three randomized, double-blind, placebo-controlled studies. A study with ten exposure sessions and drug intake 4 hours before each session failed to support the use of D-cycloserine (250 mg).[73] In contrast, significantly greater decreases in obsession-related distress after four exposure sessions under D-cycloserine (125 mg, given 2 hours before each session) were reported.[74] However, the placebo group tended to catch up after additional sessions. Both the number of therapy dropouts and the number of sessions needed to achieve "clinical milestones" were decreased by active treatment. In another study, OCD patients were reported to be significantly more improved under D-cycloserine at mid-treatment (ten behavior therapy sessions in total, dose of 100 mg 1 hour before each session), but not at later time points.[75] Dosage and timing of D-cycloserine as well as the number of combined intervensions are critical parameters. So far, just a short-term acceleration of response to exposure therapy under D-cycloserine was shown, but no significant differences in the further course due to floor effects of exposure therapy.

Several antidepressants other than SSRIs or clomipramine have been tested, as mentioned for noradrenergic tricyclics above. For the alpha-2 receptor and serotonin $(5\text{-HT})_{2/3}$ receptor antagonist mirtazapine an open trial showed negative results.[76] However, in a double-blind discontinuation period of 8 weeks (after an open trial) superiority of to placebo was demonstrated.[77] Addition of mirtazapine to citalopram did not result in increased efficacy when compared with addition of placebo, but was associated with an accelerated onset of action in a single-blind study.[78] Preclinical experiments suggest that blockade of 5-HT_{2C} receptors may have an anticompulsive effect in OCD.[79] Therefore, agomelatine, a melatonin agonist and 5-HT_{2C} antagonist, would be worth studying in OCD as well, but so far no reports have been published. The monoamino-oxidase inhibitor phenelzine was shown to be as effective as clomipramine in a double-blind trial in OCD patients,[80] while in another one it was no better than placebo.[81] A double-blind study with St John's wort (*hypericum perforatum*) failed to support efficacy for OCD.[82] Trazodone, a 5-HT_2 receptor antagonist and SRI, had shown symptomatic improvements in case series in clomipramine-resistant OCD patients[83] and in augmentation of SSRIs.[84] However, a double-blind study indicated that trazodone in monotherapy lacks substantial antiobsessive effects.[85] For selective serotonin-norepinephrine reuptake inhibitors venlafaxine and duloxetine, reliable placebo-controlled trials are still absent. In a double-blind comparison of venlafaxine and paroxetine in primary OCD patients no significant differences with regard to response or responder rates were shown.[86] In a single-blind study, venlafaxine was as efficacious as clomipramine in the acute treatment of OCD.[87] In an open retrospective investigation in treatment-resistant OCD beneficial effects of venlafaxine were demonstrated.[88] According to case series and reports switching from SSRI to duloxetine in treatment-resistant OCD patients may be helpful.[89,90] For the selective noradrenaline reuptake inhibitor reboxetine, successful augmentation of citalopram was reported in a single case.[91]

For augmentation of SSRIs with pindolol, a 5-HT_{1A} and β-adrenergic antagonist, a double-blind placebo-controlled trial found significant improvement of OCD symptoms in treatment resistant patients,[92] while an open trial only showed such effects after supplemental addition of tryptophan.[93] After double-blind primary addition of pindolol versus placebo to fluvoxamine, the latency of antiobsessional response to the SSRI was not shortened.[94] A double-blind study of adjuvant buspirone, a 5-HT_{1A} partial agonist, in OCD patients, who had shown to some extent an effect of clomipramine, did not yield significant further clinical improvement.[95] For lithium two double-blind augmentation studies have been published that do not support its usefulness in OCD. In fluvoxamine-refractory patients, a small though statistically significant reduction of OCD symptoms was reported, but the authors doubted the clinical meaningfulness of these findings.[96] A crossover study with adjuvant lithium or thyroid hormone in clomipramine-treated patients showed no significant change of OCD symptoms after either treatment.[97]

Benzodiazepine and opioid receptor ligands have been tested in OCD. A double-blind combination study of

clonazepam with sertraline did not reveal significant effects during 12 weeks of treatment.[98] While in a double-blind crossover study clonazepam in monotherapy produced a significant decrement in OCD symptoms during the first 3 weeks of treatment,[99] it was found to be without effect in a 10-week double-blind placebo-controlled trial.[100] A case of rapid remission of OCD with tramadol was reported,[101] but so far no controlled studies have been published. In treatment resistant OCD patients, who had failed two to six SRI trials, double-blind addition of once-weekly morphine resulted in a significant reduction of OCD symptoms at week two versus placebo, while lorazepam as another control condition was undistinguishable from placebo.[102] Augmentation with the opoid antagonist naltrexone did not show efficacy for OCD symptoms in a double-blind placebo-controlled study in SSRI or clomipramine refractory patients.[103]

For several other drugs preliminary interesting findings mostly from short-term open studies or case reports exist. Addition of gabapentin seems to shorten the time of onset of fluoxetine's antiobsessive effect.[104] Restarting of previously untolerated serotonergic antidepressants after valproate pretreatment was reported to lead to better tolerance and reduction of OCD symptoms in a case series.[105] Valproate monotherapy was successful in an SRI-intolerant OCD patient.[106] The 5-HT_3 receptor antagonist ondansetrone may have promise both as monotherapy[107] and as an augmentation strategy for some OCD patients.[108] Amelioration of refractory OCD on treatment with clozapine was described in a few case reports.[109-111] Antiandrogenic treatment with cyproterone acetate[112] and the long-acting gonadotropin-releasing hormone analogue triptorelin[113] was reported to result in considerable improvement of symptoms of OCD. Marked decreases of symptoms were observed shortly after single-dose exposures to the psychedelic drug psilocybin in patients with OCD.[114] Nicotine treatment was reported to display a favorable response, both in monotherapy as well as for augmentation,[115-117] while inositol augmentation of SSRIs led to a clinically significant response in some OCD patients in an open study[118]; in a small double-blind crossover study no significant improvement by this second messenger precursor was seen.[119] Acute significant antiobsessional effects for a single dose of dextroamphetamine were reported in a double-blind crossover study in patients with severe OCD.[120] Improvement of OCD was seen in treatment-resistant patients to serotonergic antidepressants after augmentation with both dextroamphetamine and caffeine in a double-blind study without placebo arm.[121]

Future prospects

Despite the considerable current knowledge that has been accumulated about evidence-based drug treatment of adults with OCD, as given account of above, and as summarized in *Table I*, several important clinical issues are still unresolved and need further research. There is still a paucity of long-term trials (especially for treatment with SRIs for more than 1 year and for augmentation with antipsychotics). Furthermore, there are as yet few switching studies, data on functional outcome parameters, combination studies of drug and cognitive behavior therapy, and randomized controlled trials with novel agents, such as glutamatergic drugs and further atypical antipsychotics.

Because of the relatively high rate of nonresponders, prediction of response to different therapeutic approaches in OCD and a further understanding of the neurobiological underpinnings of successful treatment of OCD is another important area of further research.

First-line pharmacological treatment:
• Selective serotonin reuptake inhibitors (eg, escitalopram, fluvoxamine, fluoxetine, paroxetine or sertraline) or clomipramine
• Administration of medium to high doses
• Acute treatment of at least 3 months
• If efficacious, maintenance treatment of at least 1 year
Treatment options for patients refractory to first-line pharmacological treatment:
• Modification of first-line treatment (eg, intravenous clomipramine, further dose increase, switch to other or combination of first-line drugs)
• Augmentation with antipsychotics (eg, risperidone, haloperidol, quetiapine, olanzapine, or aripiprazole)
• Augmentation with (or switch to) cognitive-behavior therapy
• Trials with other drugs (please see text)

Table I. Algorithm for drug treatment of patients with obsessive-compulsive disorder.

Currently, psychopathological or clinical parameters are not very helpful in predicting response to pharmacotherapy, not to mention in providing us with differential therapeutic support regarding which drug or therapy to choose. For treatment with SSRIs, severity and duration of OCD, psychosocial disability, earlier age at onset, older age, comorbidity with depression and personality disorder, absence of a positive family history for OCD, and poor insight, as well as neurological soft signs, were identified to predict poorer outcome.[122-129] Studies on the impact of different symptom dimensions of OCD on response to SSRIs have been equivocal, eg, while compulsive hoarding was associated with poorer response to different SSRIs in some studies,[130,131] hoarding symptoms were reported to improve as much as other symptoms of OCD after paroxetine.[132]

Concerning neurobiological markers of response and nonresponse to medication in OCD, preliminary results using endophenotyping or brain imaging have been reported. Functional polymorphisms in the serotonin system and their impact on the response to serotonergic antidepressants have yielded inconsistent results. No differences on the total OCD score in fluvoxamine response were detected in the genotype groups of the promoter region of the serotonin transporter gene *(5-HTTLPR)*,[133] as well as on treatment with different SRIs.[134] In contrast, it was reported that a significant majority of responders to paroxetine and venlafaxine carried the s/l genotype of the *5-HTTLPR* polymorphism; in OCD patients successfully treated with paroxetine response was associated with the G/G genotype of the 5-HT_{2A} receptor polymorphism.[135] Using single photon emission computed tomography (SPECT), higher pretreatment thalamus-hypothalamus serotonin transporter availability in OCD patients was found to significantly predicted better treatment response to clomipramine.[136] In a positron emission tomography (PET) study in OCD patients, local cerebral metabolic rate for glucose was significantly decreased in the head of the right caudate nucleus compared with pretreatment values in responders to fluoxetine; percentage change in OCD symptoms correlated significantly with the percent of right caudate/ipsilateral hemisphere change.[137] In another PET study, higher pretreatment regional glucose metabolism in the right caudate nucleus was shown to significantly correlate with antiobsessional response to paroxtine.[138] A significant correlation between the amelioration of OCD on treatment with serotonin reuptake inhibitors and the changes of the dopamine transporter binding ratio in the right basal ganglia was found in a SPECT study, suggesting a role in the improvement of OCD patients.[139] Distinct biological characteristics were shown in OCD patients who respond to SSRI (higher pretreatment glucose metabolism in the right caudate nucleus) and in SSRI-refractory patients, who benefit from adjunctive risperidone (higher pretreatment glucose metabolism in the right orbitofrontal cortex and bilateral thalamus).[140] Using proton magnetic resonance spectroscopy to measure N-acetyl-aspartate (NAA), a putative marker of neuronal viability, significantly lower NAA was observed in the anterior cingulate only in OCD patients who responded to the combination therapy of SSRI plus atypical antipsychotic.[141]

Whether these exciting new developments will ultimately further advance our understanding of the neurobiology and effective psychopharmacology of OCD, and whether some of them will eventually enter clinical practice to serve our OCD patients, still needs to be established. ❑

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Tratamiento farmacológico del trastorno obsesivo-compulsivo

En los últimos 40 años ha habido un importante aumento del conocimiento de las opciones de farmacoterapia para el trastorno obsesivo-compulsivo (TOC). Los antidepresivos serotoninérgicos, como los inhibidores selectivos de la recaptura de serotonina (ISRS) y la clomipramina, se consideran los tratamientos farmacológicos de primera línea en el tratamiento del TOC. Se recomienda el empleo de dosis intermedias o altas y un tratamiento agudo de al menos tres meses antes de evaluar la eficacia. En el caso de una mejoría significativa es necesario el tratamiento de mantenimiento. Es lamentable que cerca de la mitad de los pacientes no responda suficientemente a antidepresivos serotoninérgicos orales, por lo que la potenciación con antipsicóticos atípicos es una estrategia de tratamiento farmacológico de segunda línea. Otras alternativas incluyen los antidepresivos serotoninérgicos intravenosos y la combinación con una psicoterapia cognitivo conductual o un cambio a esta última. Es destacable que un porcentaje considerable de pacientes con TOC aun no recibe un tratamiento farmacológico racional. Se revisan aproximaciones novedosas de la investigación, como los estudios terapéuticos preliminares con sustancias glutamatérgicas, y los ensayos con otros fármacos, al igual que algunos aspectos de la investigación futura.

Traitement pharmacologique des troubles obsessionnels compulsifs

Ces 40 dernières années ont vu s'améliorer de manière importante la connaissance du traitement pharmacologique du trouble obsessionnel compulsif (TOC).. Les antidépresseurs sérotoninergiques, comme les inhibiteurs sélectifs de la recapture de la sérotonine (ISRS) et la clomipramine, représentent le traitement pharmacologique de première ligne reconnu pour les TOC. Des posologies moyennes à fortes sont nécessaires, avec une phase aiguë d'au moins 3 mois pour obtenir des résultats et en cas d'amélioration significative, un traitement d'entretien est nécessaire. Malheureusement, environ la moitié des patients ne répondent pas suffisamment aux antidépresseurs sérotoninergiques oraux. La stratégie thérapeutique de deuxième intention consiste alors à additionner des antipsychotiques atypiques. L'administration d'antidépresseurs sérotoninergiques intraveineux et l'association ou le passage à la psychothérapie cognitivocomportementale sont des alternatives possibles. Étonnamment, un pourcentage considérable de patients atteints de TOC ne reçoit pas encore de traitement adapté. Nous analysons dans cet article les nouvelles démarches concernant la recherche, comme les études thérapeutiques préliminaires avec des substances glutamatergiques, les essais avec d'autres médicaments ainsi que certaines perspectives nécessaires à la recherche future.

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