

# Psychogenic Excoriation

## Clinical Features, Proposed Diagnostic Criteria, Epidemiology and Approaches to Treatment

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### Abstract

Psychogenic excoriation (also called neurotic excoriation, acne excoriée, pathological or compulsive skin picking, and dermatotillomania) is characterised by excessive scratching or picking of normal skin or skin with minor surface irregularities. It is estimated to occur in 2% of dermatology clinic patients and is associated with functional impairment, medical complications (e.g. infection) or substantial distress.

Psychogenic excoriation is not yet recognised in the DSM. We propose preliminary operational criteria for its diagnosis that take into account the heterogeneity of behaviour associated with psychogenic excoriation and allow for subtyping along a compulsivity-impulsivity spectrum.

Psychiatric comorbidity in patients with psychogenic excoriation, particularly mood and anxiety disorders, is common. Patients with psychogenic excoriation frequently have comorbid disorders in the compulsivity-impulsivity spectrum, including obsessive-compulsive disorder, body dysmorphic disorder, substance use disorders, eating disorders, trichotillomania, kleptomania, compulsive buying, obsessive-compulsive personality disorder, and borderline personality disorder.

There are few studies of the pharmacological treatment of patients with psychogenic excoriation. Case studies, open trials and small double-blind studies

have demonstrated the efficacy of selective serotonin (5-hydroxytryptamine; 5-HT) reuptake inhibitors in psychogenic excoriation. Other pharmacological treatments that have been successful in case reports include doxepin, clomipramine, naltrexone, pimozone and olanzapine.

There are no controlled trials of behavioural or psychotherapeutic treatment for psychogenic excoriation. Treatments found to be effective in case reports include a behavioural technique called 'habit reversal'; a multicomponent programme consisting of self-monitoring, recording of episodes of scratching, and procedures that produce alternative responses to scratching; and an 'eclectic' psychotherapy programme with insight-oriented and behavioural components.

## 1. Clinical Features

Psychogenic excoriation is characterised by excessive scratching, picking, gouging, lancing, digging, rubbing or squeezing of normal skin or skin with minor surface irregularities. Skin lesions such as acne, papules, scabs, scars, calluses and insect bites are sometimes excoriation sites.<sup>[1-5]</sup> Excoriation may also occur in response to pruritus or other skin sensations such as burning, crawling, tingling, warmth, prickling, dryness and pain.<sup>[1,3]</sup> Most patients excoriate skin with their fingernails and fingers, but the teeth and instruments (e.g. tweezers, nail files, pins or knives) are also sometimes used.<sup>[2-5]</sup> Excoriations are usually found in areas that are easily reachable, and most patients excoriate multiple sites. The face is the most common site of excoriation.<sup>[3,4]</sup> Excoriations are typically a few millimetres in diameter and weeping, crusted or scarred with occasional postinflammatory hypopigmentation or hyperpigmentation.<sup>[6]</sup>

## 2. Diagnosis

The behaviour associated with psychogenic excoriation is heterogeneous and spans a compulsivity-impulsivity continuum from obsessive-compulsive disorder (OCD) symptoms to impulse control disorder symptoms, with mixed features in between.<sup>[3]</sup> Most patients report symptoms of an impulse control disorder in that they find themselves acting automatically and experience an increase in tension prior to excoriating and transient relief or pleasure either with or immediately after excoriating.<sup>[2-4]</sup> In contrast, the behaviour sometimes has features of OCD when it is ritualistic, often resisted and ego-dystonic.<sup>[7]</sup>

Some patients describe obsessions about an irregularity on the skin or preoccupation with having smooth skin and excoriate in response to the thoughts.

A preoccupation with appearance can be severe enough to also meet criteria for body dysmorphic disorder (BDD), a disorder thought to be related to OCD.<sup>[8]</sup> In one case series of patients with psychogenic excoriation, the subgroup of patients who met criteria for BDD also had symptoms of an impulse control disorder.<sup>[3]</sup> The majority of patients with psychogenic excoriation have both impulsive and compulsive features, a finding common in patients with trichotillomania.<sup>[9]</sup>

Although psychogenic excoriation is not yet recognised in the DSM-IV,<sup>[10]</sup> we propose preliminary operational criteria for its diagnosis based on a number of studies of the phenomenology of patients with this syndrome<sup>[1-5]</sup> (table I). These criteria take into account the heterogeneity of behaviour associated with psychogenic excoriation and allow for subtyping along a compulsivity-impulsivity spectrum. This categorisation of the disorder into compulsive, impulsive and mixed subtypes has never been done for psychogenic excoriation or other related DSM-IV disorders such as trichotillomania, but we believe this innovative method of categorisation better reflects the heterogeneity of these disorders and deserves more study. Furthermore, the identification of compulsive, impulsive and mixed subtypes has important treatment implications as the presenting phenomenology may predict pharmacological responsiveness as discussed in section 7.

Psychogenic excoriation has also been called neurotic excoriation, acne excoriée, skin picking, patho-

**Table I.** Proposed diagnostic criteria for psychogenic excoriation

A. Maladaptive skin excoriation (e.g. scratching, picking, gouging, lancing, digging, rubbing or squeezing skin) or maladaptive preoccupation with skin excoriation as indicated by at least 1 of the following:

- preoccupation with skin excoriation and/or recurrent impulses to excoriate the skin that is/are experienced as irresistible, intrusive and/or senseless
- recurrent excoriation of the skin resulting in noticeable skin damage

B. The preoccupation, impulses or behaviours associated with skin excoriation cause marked distress, are time-consuming, significantly interfere with social or occupational activities, or result in medical problems (e.g. infections)

C. The disturbance is not better accounted for by another mental disorder and is not due to a general medical condition

#### Subtypes

##### *Compulsive type*

Skin excoriation is performed to avoid increased anxiety or to prevent a dreaded event or situation and/or is elicited by an obsession (e.g. obsession about contamination of the skin)

It is performed in full awareness

It is associated with some resistance to performing the behaviour

There is some insight into its senselessness or harmfulness

##### *Impulsive type*

Skin excoriation is associated with arousal, pleasure or reduction of tension

It is performed at times with minimal awareness (e.g. automatically)

It is associated with little resistance to performing the behaviour

There is little insight into its senselessness or harmfulness

##### *Mixed type*

Skin excoriation has both compulsive and impulsive features

logical or compulsive skin picking, and dermatotillomania. We prefer the term psychogenic excoriation for several reasons. First, excoriation is the term used in the dermatological literature and is broader than the terms skin picking and acne excoriée. Secondly, psychogenic implies a psychiatric cause for the excoriation. Thirdly, compulsive skin picking is too suggestive of OCD and does not take into account the heterogeneity of the behaviour associated with excoriation. Finally, neurotic is a term that has been phased out of the DSM. Dermatotillomania may also be an acceptable name for the disorder, as it may underscore the similarities between this disorder and trichotillomania.<sup>[11]</sup>

Although most patients with skin sensations associated with excoriation develop compulsive-im-

pulsive behaviours that are independent of the sensations,<sup>[3]</sup> a minority of patients excoriate skin only in response to sensations such as pruritus. These patients may have an underlying dermatological condition that better accounts for the skin excoriation. Alternatively, their symptoms may meet criteria for an undifferentiated somatoform disorder (e.g. idiopathic pruritus) if the skin sensations cannot be explained by a known medical condition or are in excess of what would be expected from a specific medical condition.<sup>[3]</sup>

### 3. Epidemiology

The lifetime prevalence rate of psychogenic excoriation in the general population is unknown, but it is estimated to occur in about 2% of dermatology clinic patients<sup>[12]</sup> and was found in 3.8% of a non-clinical sample of college psychology students.<sup>[5]</sup> Pooled results from 3 of the largest case series of patients with psychogenic excoriation show a female to male ratio of about 8 : 1.<sup>[1,3,4]</sup> However, this ratio may reflect differences in treatment seeking between women and men. Thus, although psychogenic excoriation appears to be more common in women, confirmation of the gender distribution with community samples is needed. More Caucasian than African-American individuals have presented for studies of psychogenic excoriation,<sup>[3]</sup> but this may not be representative of the racial distribution of psychogenic excoriation in the general population.

### 4. Course

The mean age of onset of psychogenic excoriation ranges from 15 to 45 years.<sup>[1-4,13]</sup> The mean duration of symptoms also has a wide range of between 5 and 21 years.<sup>[1-4,13]</sup>

Most patients spend a total of 3 hours or less a day excoriating the skin, and there is a wide range of behavioural patterns, from multiple brief episodes of excoriation to less frequent episodes of several hours' duration.<sup>[2,3]</sup> For many patients, skin excoriation is worse in the evening, from 2000h to 2400h.<sup>[4]</sup>

Most patients engage in the behaviour continuously during the course of the disorder without prolonged breaks, although some do it intermittently with periods of months to years free of the behaviour.<sup>[2]</sup> The prognosis for patients who have had psychogenic excoriation for less than 1 year before presenting to a dermatologist appears to be better than for those with a longer duration of illness.<sup>[1]</sup>

## 5. Functional Impairment

Psychogenic excoriation causes substantial distress, and most patients describe embarrassment or shame about the behaviour and have difficulty revealing their 'secret' to doctors or close associates.<sup>[2]</sup> In addition, most patients report impairment in social functioning as a result of the behaviour.<sup>[2-4]</sup> Avoidance of activities that might expose their skin lesions to others contributes to restriction in activities such as sexual activity and leisure or sports events.<sup>[2]</sup> A small number of patients withdraw from most social activities altogether and confine themselves to their homes.<sup>[3]</sup> Most patients resort to cosmetics, clothing and/or bandages to camouflage their skin lesions.<sup>[3,4]</sup>

Medical complications are varied and include soreness, bleeding, temporarily large excoriations, ulcers, infections, permanent discoloration and scarring that can be disfiguring.<sup>[2-4]</sup> Marked dissatisfaction with the appearance of the skin after excoriation is common.<sup>[4]</sup>

## 6. Comorbidity

Psychiatric comorbidity, particularly mood and anxiety disorders, is common in patients with psychogenic excoriation.<sup>[3,4]</sup> Current mood disorders, including major depression, bipolar disorder and dysthymia, are found in 48 to 68% of patients with psychogenic excoriation, and current anxiety disorders, including panic disorder, agoraphobia, social and specific phobia, OCD, post-traumatic stress disorder and generalised anxiety disorder, are found in 41 to 65% of patients.<sup>[3,4]</sup>

Mood and anxiety disorders are also frequently comorbid with other core disorders in the compulsive-impulsive spectrum.<sup>[14]</sup> Furthermore, compulsive-

impulsive spectrum disorders in addition to OCD that are frequently found in patients with psychogenic excoriation include psychoactive substance use disorders, BDD, eating disorders and the impulse control disorders trichotillomania, kleptomania and compulsive buying.<sup>[3,4]</sup> For example, patients with a preoccupation with skin appearance that meets criteria for BDD could also have a preoccupation with skin excoriation and meet criteria for psychogenic excoriation as proposed in table I. Personality disorders are also common, occurring in 71% of one sample of patients with psychogenic excoriation, with obsessive-compulsive personality disorder the most common, followed by borderline personality disorder.<sup>[4]</sup> Both of these personality disorders are also considered impulsive-compulsive core disorders.<sup>[15]</sup>

The high comorbidity of psychogenic excoriation with impulsive-compulsive core disorders provides further evidence that the behaviour associated with psychogenic excoriation spans a compulsivity-impulsivity spectrum. However, more study is needed to support the compulsive-impulsive spectrum model for psychogenic excoriation.

## 7. Treatment

### 7.1 Pharmacotherapy

There are few studies examining the pharmacological treatment of patients with psychogenic excoriation (table II). Case studies, open trials and small double-blind studies have demonstrated the efficacy of selective serotonin (5-hydroxytryptamine; 5-HT) reuptake inhibitors (SSRIs) in psychogenic excoriation. A double-blind, placebo-controlled 10-week trial of fluoxetine using a flexible dose schedule up to 80 mg/day in 21 patients with psychogenic excoriation found that the drug, at a mean dosage of 55 mg/day, was significantly superior to placebo in reducing skin excoriation. There was no relationship between skin-picking improvement and changes in measures of depression, anxiety and obsessive-compulsive symptoms, suggesting that the effect of fluoxetine on skin picking was a primary one.<sup>[2]</sup>

**Table II.** Studies of the pharmacological treatment of psychogenic excoriation

Reference(s)	Drug	Study design (no. of patients)	Mean dosage (range) [mg/day]	Conclusions
Simeon et al. <sup>[2]</sup>	Fluoxetine	Double-blind, placebo-controlled (21)	55 (20-80)	Significant reduction in skin-picking behaviour
Bloch et al. <sup>[16]</sup>	Fluoxetine	Open-label followed by double-blind, placebo-controlled continuation trial (15)	41 (20-60)	Open treatment effective in reducing skin picking in 8 of 15 patients; significant improvement maintained in the double-blind phase
Phillips & Taub, <sup>[8]</sup> Stout, <sup>[17]</sup> Gupta & Gupta, <sup>[18]</sup> Stein et al., <sup>[19]</sup> Vittorio & Phillips <sup>[20]</sup>	Fluoxetine	Case reports	(20-80)	Effective reduction of skin excoriation in multiple case reports
Kalivas et al. <sup>[21]</sup>	Sertraline	Uncontrolled series (28)	95 (25-200)	19 (68%) patients showed $\geq 50\%$ reduction in open skin lesions
Arnold et al. <sup>[22]</sup>	Fluvoxamine	Uncontrolled series (14)	112.5 (25-300)	Significant reduction in skin excoriation
O'Sullivan et al. <sup>[23]</sup>	Fluvoxamine	Case report	300	Reduced skin picking and preoccupation with skin appearance in patient with body dysmorphic disorder
Biondi et al., <sup>[24]</sup> Ravindran et al. <sup>[25]</sup>	Paroxetine	Case reports	(30-40)	Decrease in pruritus and skin excoriation
Harris et al. <sup>[26]</sup>	Doxepin	Case report	30	Decrease in pruritus and skin excoriation
Gupta et al. <sup>[13]</sup>	Clomipramine	Case report	50	Decrease in pruritus and skin excoriation
Lienemann & Walker <sup>[27]</sup>	Naltrexone	Case report	50	Resolution of skin excoriation
Duke <sup>[28]</sup>	Pimozide	Case reports	4	Resolution of skin excoriation after 1 mo of treatment
Garnis-Jones et al., <sup>[29]</sup> Gupta & Gupta <sup>[30]</sup>	Olanzapine	Case reports	(2.5-7.5)	Resolution of skin excoriation with olanzapine either alone or as adjunctive treatment to antidepressants

Open-label fluoxetine at a mean dosage of 41 mg/day for 6 weeks was effective in reducing skin excoriation in 8 of 15 individuals. The 8 responders were then randomised to 6 weeks of double-blind fluoxetine at the highest tolerated dosage or to placebo continuation treatment. The double-blind placebo substitution was associated with relapse within 6 weeks.<sup>[16]</sup>

Case reports have demonstrated that fluoxetine is effective within 2 to 4 weeks at dosages of 20 mg/day<sup>[18-20]</sup> and 40 mg/day.<sup>[17]</sup> Fluoxetine at a dosage of 80 mg/day produced 'near remission' of skin picking associated with BDD over the course of 3 years in a patient who had not previously responded to trials of psychotherapy, cognitive-behavioural therapy, imipramine, amitriptyline or benzopidiazepines.<sup>[8]</sup>

In an open trial, sertraline, started at 25 to 50 mg/day and increased to 100 to 200 mg/day, was

found to be effective in 19 of 28 (68%) patients with psychogenic excoriation. The responders received a mean daily dose of 95 mg/day and experienced a 50% or greater reduction in open skin lesions by 1 month of treatment.<sup>[21]</sup>

Fluvoxamine, at a mean dosage of 112.5 mg/day, was found to significantly reduce behaviours involving the skin in a 12-week open trial of 14 patients.<sup>[22]</sup> The reduction in skin-related behaviours was independent of mood, which is consistent with the double-blind study of fluoxetine in the treatment of skin picking,<sup>[2]</sup> suggesting that the medication had a primary effect on the behaviour.<sup>[22]</sup> A patient with skin picking secondary to BDD and delusional disorder, somatic type, responded to treatment with fluvoxamine 300 mg/day, with lessening of both picking behaviour and preoccupation with skin appearance.<sup>[23]</sup>

Paroxetine begun at 20 mg/day for 3 weeks and increased to 30 mg/day for another 3 weeks led to resolution of idiopathic pruritus (undifferentiated somatoform disorder) and skin excoriation in a patient who had not responded to treatment with conventional antipruritic drugs. The patient maintained improvement at 9 months follow-up.<sup>[24]</sup> Another patient, in whom trials of dermatological topical preparations, psychotherapy and treatment with lorazepam (up to 3 mg/day) and trazodone (50 mg/day) had failed, experienced resolution of skin picking that was associated with 'itchiness' on paroxetine, started at 20 mg/day and increased to 40 mg/day for 4 months. The improvement was maintained at 1-year follow-up.<sup>[25]</sup>

Other pharmacological approaches to the treatment of psychogenic excoriation include doxepin, which reduced both pruritus and excoriation in 1 patient at a dosage of 30 mg/day after 3 weeks. With the addition of outpatient psychotherapy to doxepin for 6 months, the skin lesions had healed with some scarring.<sup>[26]</sup> Clomipramine started at 25 mg/day and increased to 50 mg/day after 1 week led to improvement in pruritus and excoriation within the first week and marked improvement after 3 weeks in a patient whose symptoms had not responded to 4.5 years of treatment with antihistamines and topical corticosteroids.<sup>[13]</sup>

An orally active opiate antagonist, naltrexone, at 50 mg/day reduced skin picking and pruritus in a patient whose symptoms had not responded to treatment with prednisone 20 mg/day, topical corticosteroids, psoralen plus UVA treatments or phenelzine 45 mg/day.<sup>[27]</sup> Interestingly, before treatment with naltrexone, the patient had not experienced pain while scratching as occurs in many patients with psychogenic excoriation.<sup>[31]</sup> After 3 days of naltrexone the patient noticed pain with skin picking, and after 8 days the skin excoriation resolved and over the next 28 days the lesions healed. Naltrexone may work by blocking the endogenous reward from release of opioids that may occur with skin excoriation.<sup>[27]</sup>

There are several case reports supporting the efficacy of the antipsychotics pimozide<sup>[28]</sup> and, more

recently, olanzapine in the treatment of psychogenic excoriation.<sup>[29,30]</sup> Pimozide 4 mg/day was given to 2 patients with severe psychogenic excoriation, both of whom experienced clearing of all lesions after 1 month of treatment.<sup>[28]</sup> Olanzapine was effective in 3 nonpsychotic patients with psychogenic excoriation.<sup>[29]</sup> The first patient was receiving treatment with nefazodone for comorbid social phobia, but this treatment had no effect on the excoriation. The addition of olanzapine 7.5 mg/day reduced his urges to excoriate the skin. The second patient experienced relief of psychogenic excoriation with 2.5 mg/day of olanzapine along with isotretinoin for facial acne. The last patient had comorbid depression and OCD treated with fluvoxamine 300 mg/day without improvement of the psychogenic excoriation. Adjunctive olanzapine 7.5 mg/day led to a resolution of the excoriation. In the second case series of olanzapine treatment of psychogenic excoriation, 2 patients with psychogenic excoriation improved after a 2- to 4-week course of olanzapine at a dosage of 2.5 to 5.0 mg/day.<sup>[30]</sup>

More studies are needed to confirm the responsiveness of psychogenic excoriation to pharmacological treatments. No study has determined whether the presence of compulsive and/or impulsive features predicts treatment response. It may be that those with more compulsive features respond to SSRIs, and those with impulsive features respond to a wider range of antidepressants, mood stabilisers or antipsychotics.<sup>[14]</sup> More study is also needed to determine how comorbid disorders such as bipolar disorder affect treatment response.

## 7.2 Behavioural Treatment and Psychotherapy

There are no controlled trials of behavioural or psychotherapeutic treatments for psychogenic excoriation. One behavioural treatment reported to be effective in case reports is a technique called 'habit reversal'.<sup>[32,33]</sup> This involves several steps:<sup>[32,33]</sup>

1. *Response description*: the patient describes and demonstrates the scratching behaviour to the clinician.

2. *Early warning*: the patient is taught to detect movement of the hand to areas of excoriation.
3. *Situation awareness training*: the patient describes when the excoriation occurs to increase awareness of situations or stressors associated with the behaviour.
4. *Habit inconvenience review*: unpleasant consequences of the excoriation are reviewed to increase motivation to stop the behaviour.
5. *Competing response practice*: patients are taught an isometric exercise that is incompatible with scratching, such as clenching the fists for at least 1 minute; the patient is instructed to perform the competing response when any urge to scratch or scratching occurs.
6. *Generalisation training*: the patient is taught to perform the competing response without disruption in usual activities.
7. *Symbolic rehearsal*: the patient practises the competing response in the presence of the clinician.

In one case report, a patient who excoriated acne and had not responded to treatment with a variety of topical agents experienced a marked reduction in the urge to excoriate and a reduction in picking behaviour after 1 month of habit reversal practice. The improvement was maintained at the 4-month follow-up.<sup>[33]</sup> In 4 patients who underwent habit reversal training in a single 1-hour session, scratching was eliminated for 1 patient and decreased for the other 3 patients at 6 months follow-up.<sup>[32]</sup>

Other behavioural treatments for psychogenic excoriation include a multicomponent programme consisting of self-monitoring and recording of scratching episodes, stimulus control procedures that produce alternative responses to scratching, and functional analyses. The goal of this approach is to separate the scratching behaviour into its component elements and provide instruction for controlling these elements.<sup>[34]</sup> A patient with excoriation and pruritus whose symptoms had not responded to treatment with topical treatments, antihistamines or doxepin (75 mg/day) responded to this multicomponent programme with a marked decrease in scratching episodes over a 12-week period. The

**Table III.** Guidelines for the evaluation and treatment of psychogenic excoriation

#### Evaluation

Obtain a detailed history of the excoriation episodes:

- location of excoriation
- timing (e.g. age excoriation began and the course of the problem, the frequency and duration of episodes, and the time of the day they occur)
- method of excoriation (e.g. use of fingers, instrumentation, etc.)
- severity of excoriation (e.g. medical complications)
- precipitants to excoriation (e.g. any stressors, triggers, or skin sensations)
- context of excoriation (e.g. situations in which it occurs)
- modifying factors (e.g. what makes the excoriation better or worse)
- thoughts and emotions before, during and after excoriation

Assess for impulsive and/or compulsive features

Ensure adequate dermatological evaluation and assess for other

underlying medical or psychiatric causes for the disturbance

Evaluate for comorbid psychiatric disorders

#### Treatment

Refer for dermatological evaluation if an underlying medical disorder is suspected

Treat any underlying psychiatric disorders (e.g. body dysmorphic disorder or delusional disorder)

Treat any comorbid psychiatric disorders (e.g. mood and anxiety disorders)

Consider a trial of a selective serotonin reuptake inhibitor, particularly in patients with prominent compulsive features

Consider a trial of a tricyclic antidepressant such as doxepin in patients with prominent pruritus

If antidepressants are ineffective, consider a trial of naltrexone or olanzapine

Consider a trial of habit reversal

improvement was stable at the follow-up evaluation after 6 months.<sup>[34]</sup>

There are case reports and case series of successful treatment of psychogenic excoriation with psychotherapy.<sup>[6]</sup> Healing of skin lesions occurred in 17 (85%) of 20 patients with psychogenic excoriation who underwent an 'eclectic' psychotherapy programme with insight-oriented and behavioural components compared with in 15 (24%) of 63 patients who received only social advice and support.<sup>[35]</sup> Others have proposed a '3-level approach' to the treatment of psychogenic excoriation, including lesional (e.g. occlusional, topical or intralesional therapies), emotional (e.g. a strong doctor-patient

alliance) and cognitive (e.g. offering the patient alternative behaviours for scratching) options that can be combined with one another and with medications.<sup>[36]</sup>

Guidelines for the evaluation and treatment of patients with psychogenic excoriation are summarised in table III.

## 8. Conclusion

The evaluation of patients with psychogenic excoriation includes a thorough history of the excoriation episodes, an assessment for impulsive or compulsive features, and a dermatological and psychiatric evaluation to assess for other underlying or comorbid medical or psychiatric disorders. If the disturbance is better accounted for by another psychiatric disorder (e.g. delusions of parasitosis) or general medical condition (e.g. atopic dermatitis), treatment of these disorders may lead to a resolution of the skin excoriation. Once other causes of the skin excoriation have been ruled out, treatment of psychogenic excoriation should address comorbid psychiatric disorders and the presence of compulsive or impulsive features. For example, patients with prominent compulsive features and comorbid disorders such as major depression or BDD may respond preferentially to the SSRIs. Behavioural treatment or psychotherapy may also be considered as adjunctive therapy in those patients whose symptoms do not respond to medication alone.

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