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**Review Article**

# Therapy of somatoform disorders

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**Abstract**

Somatoform disorders are categorized in the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR) under the following categories: Somatization Disorder, Undifferentiated Somatoform Disorder, Conversion Disorder, Pain Disorder, Hypochondriasis, Body Dysmorphic Disorder and Somatoform Disorder Not Otherwise Specified (NOS). As a group they are characterized by the presence of physical symptoms that suggest a general medical condition and they must cause clinically significant distress or impairment of social, occupational or other areas of functioning. Evidence suggests that somatoform symptoms account for a significant percentage of primary care consultations. However, their inclusion in DSM-IV-TR as a discrete diagnostic category is controversial. This may explain the small number of treatment studies conducted in the majority of categories of the somatoform disorders. The definition of populations for research studies remains a challenge, as do valid response criteria, because of the heterogeneous populations of subjects with varying co-morbid disorders. As a result, there are very few validated assessment scales. The notable exception to the poorly researched categories is body dysmorphic disorder. Mainly as a result of studies conducted within the Body Dysmorphic Disorder and Body Image Program based in Rhode Island, USA, we now have a better understanding of the disorder and evidence for the efficacy of selective serotonin reuptake inhibïtors (SSRIs) in its treatment.

## Introduction

Somatoform disorders are a group of psychiatric disorders characterized by the presence of physical symptoms that suggest a general medical condition. This group of disorders is categorized in the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR) (1) under the following categories: Somatization Disorder, Undifferentiated Somatoform Disorder, Conversion Disorder, Pain Disorder, Hypochondriasis, Body Dysmorphic Disorder and Somatoform Disorder Not Otherwise Specified (NOS). According to DSM-IV-TR, the symptoms of somatoform disorders must cause clinically significant distress or impairment of social, occupational or other areas of functioning, and not be fully explained by a general medical condition, by the direct effects of a substance or by another mental disorder. The inclusion of somatoform disorders as a diagnostic category in DSM during the 1980s is controversial, mainly due to the borderline nature of the symptoms between somatic (general) medicine and psychiatry. Although the scientific literature includes numerous articles referring to somatoform disorders, their validity and applicability in clinical and research settings have been questioned because of the debate regarding the underlying classification of the disorders (2-4).

Somatic symptoms which cannot be fully explained by a general medical condition are known to be widely prevalent in general practice and in primary care settings, and studies have shown that such symptoms may account for 25-50% of all patient visits (5). However, the prevalence of the disorders varies widely depending on the diagnostic criteria from DSM-IV-TR, with relatively low rates for hypochondriasis and somatization disorder, for example (6). There is considerable evidence that these two categories in particular are so closely linked to anxiety and depressive disorders that their distinction from them is difficult to evaluate. Indeed, a number of studies have reported substantial co-morbidity between somatoform and other mental disorders. In a 2-stage prevalence study conducted in 8 university-affiliated general practices in The Netherlands, which included a standardized diagnostic interview in 473 patients, the prevalence of somatoform disorders was 16%. The co-morbidity of somatoform disorders with anxiety or depressive disorders was 3.3 times more likely than would have been expected by chance, with 54% of patients with an anxiety and/or depressive disorder also having a somatoform disorder. In this study, physical, depressive and functional symptoms were found to be additive in patients with such co-morbid disorders (7).

Multiple strategies have been used for the treatment of somatoform disorders, including psychosocial treat-

ments, pharmacotherapy and educational interventions. Pharmacological treatments are considered to have a limited role because the physical symptoms of patients with somatoform disorders often become chronic and refractory to treatment. Patients also have a high risk of tolerance and dependence. The successful management of these patients therefore presents a challenge to primary care physicians and general practitioners alike, and a combination of therapy and intervention is frequently used (5). The present review focuses on pharmacotherapy options in the management of the various categories of somatoform disorders (see Table I).

## Somatization disorder, undifferentiated somatoform disorder and somatoform disorder NOS

Somatization disorder is a polysymptomatic disorder characterized by a combination of pain, gastrointestinal, sexual and pseudoneurological symptoms. The multiple somatic complaints must begin before 30 years of age and occur over a period of several years. Major depressive disorder, panic disorder, substance-related disorders and personality disorders are frequent co-morbidities in individuals with somatization disorder. Lifetime prevalence rates of 0.2-2% among women and < 0.2% in men have been reported for somatization disorder (1). Somatoform presentations that do not meet the criteria for somatization disorder are classified as undifferentiated somatoform disorder when one or more physical complaints persist for 6 months or longer. In the aforementioned Dutch study (7), undifferentiated somatoform disorder was the most common somatoform disorder, with a prevalence of 13%. Somatoform disorder NOS is used to describe somatoform symptoms that do not meet the criteria for any specific somatoform disorder and are of < 6 months' duration (1).

Despite the widespread prevalence of undifferentiated somatoform disorder, in particular in primary care settings, little data exist on the efficacy of pharmacotherapy in this and other somatoform presentations. The efficacy of the tricyclic compound opipramol 200 mg/day was evaluated in a randomized, placebo-controlled trial in 200 patients. In this study, somatoform disorders were classified according to the International Classification of Diseases (ICD-10) (8). Opipramol was significantly more effective than placebo on the primary efficacy parameter —improvement in the somatic subscore of the Hamilton Anxiety Scale (HAMA)— and on the majority of other outcome criteria (9).

Two randomized, placebo-controlled trials evaluated the efficacy of St. John's wort (*Hypericum*) extract (LI-160) in somatoform disorders. In a 6-week trial, 151 outpatients with somatization disorder, undifferentiated somatoform disorder or somatoform autonomic dysfunctions (according to ICD-10) received LI-160 at a dose of 600 mg/day or placebo. The primary outcome measure was the somatic anxiety subscore of HAMA. The decrease in this subscore was statistically significantly greater in the LI-160 group than in the placebo group. Superior efficacy was also demonstrated for LI-160 on secondary efficacy criteria, including Clinical Global Impression (CGI) score and HAMA total score. Efficacy was independent of existing depressive symptoms and the treatment was well tolerated (10).

A further prospective, randomized, double-blind, placebo-controlled study was performed in 184 outpatients with somatization disorder, undifferentiated somatoform disorder or somatoform autonomic dysfunctions without significant co-morbid depression. Patients received LI-160 600 mg/day or placebo for 6 weeks. In this study, a new 53-item instrument for the evaluation of treatment effects in somatoform disorders, the Screening for Somatoform Symptoms-7 (SOMS-7), was used. This had been previously validated in a group of 325 patients (11). The superiority of LI-160 was statistically significant compared with placebo when assessed by the six variables chosen for the primary efficacy analysis, and also for a combined measure. In addition, 45% of patients who received LI-160 were classified as responders compared with 21% of those who received placebo. Similar proportions of patients considered themselves to be "completely improved" at the end of the treatment period (44% *versus* 25%) (12).

The efficacy of the selective dopamine antagonist amisulpride was also evaluated in 32 patients with a range of somatoform disorders, 19 of whom had undifferentiated somatoform disorder. Other diagnoses were pain disorder, hypochondriasis and somatization disorder. Amisulpride was administered at low doses (50-100 mg/day) for 6 weeks. At these doses, amisulpride exerts dopamine-agonist activity and has been used in the treatment of clinical depression. There was a significant decrease in the somatic anxiety subscore of HAMA after 1 week of treatment, and after 6 weeks both the Hamilton Depression Rating Scale (HAMD) and HAMA total score for depression were improved (13).

## Conversion disorder

Conversion disorder is defined by the presence of symptoms or deficits affecting voluntary motor or sensory function that suggest a neurological or other general medical condition. The presence of a neurological condition does not preclude a diagnosis of conversion disorder; indeed, as many as one-third of individuals with conversion symptoms have a current or prior neurological condition. Subtypes of conversion disorder are defined based on the nature of the presenting symptoms or deficits, and recurrence of symptoms is common. Women presenting with conversion disorder may later develop somatization disorder, although this rarely occurs in men. Men, however, are more likely to exhibit antisocial personality disorder in association with conversion disorder. The prevalence of conversion disorder has been reported to be up to 3% in outpatient referrals to mental health clinics (1).

The importance of identifying and treating the underlying psychiatric disorder associated with conversion disorder has been highlighted. Follow-up studies of patients

*Table I: Completed and ongoing studies of experimental therapies for somatoform disorders (continuously updated information available in Prous Science Integrity®).*

| Indication | Design | Treatments | n | Conclusions | Ref. |
|---|---|---|---|---|---|
| Somatization disorder | Randomized<br>Double-blind<br>Placebo-controlled | Opipramol, 200 mg/d p.o. [titrated from 50 mg/d over 3 d] x 6 wks<br>Placebo | 200 | Opipramol was effective for the treatment of somatoform disorders | 9 |
| | Randomized<br>Double-blind<br>Placebo-controlled | St. John's wort extract, 300 mg p.o. b.i.d. x 6 wks<br>Placebo | 151 | St. John's wort extract showed excellent tolerability and efficacy for the treatment of somatoform disorders. The effect was independent of the existence of depressive mood | 10 |
| | Randomized<br>Double-blind<br>Placebo-controlled | St. John's wort extract, 300 mg p.o. b.i.d. x 6 wks<br>Placebo | 184 | Daily treatment with 600 mg of St. John's wort extract was safe and effective for the treatment of somatoform disorders | 12 |
| | Open | Amisulpride, 50-100 mg/d p.o. x 6 wks | 32 | Amisulpride was safe and effective in patients with somatoform disorders | 13 |
| Conversion disorder | Open | Citalopram, 40 [max.] mg/d [titrated from 10 mg/d] x 8 wks → [if no response @ 4 wks] Venlafaxine, 300 [max.] mg/d [titrated from 37.5 mg/d]<br>Paroxetine, 40 [max.] mg/d [titrated from 10 mg/d] x 8 wks → [if no response @ 4 wks] Venlafaxine, 300 [max.] mg/d [titrated from 37.5 mg/d] | 15 | Antidepressant therapy with citalopram, paroxetine or venlafaxine could be effective for the treatment of chronic psychogenic movement disorders with primary conversion symptoms | 16 |
| | Randomized<br>Double-blind<br>Placebo-controlled | Sertraline, 200 [max.] mg/d [titrated from 25 mg/d over 4 wks according to tolerability] x 12 wks<br>Placebo | 50 | A clinical study was initiated to evaluate sertraline in patients with psychogenic nonepileptic seizures. The study will obtain outcome data and the effect size necessary for a future randomized, controlled trial | 17 |
| Pain disorder | Open | Moclobemide, 450 mg/d p.o. [titrated from 300 mg/d] x 8 wks | 14 | Moclobemide was an effective and useful therapeutic option for the treatment of perceived pain in patients with somatoform disorder and also improved depression, somatization and anxiety | 18 |
| | Comparative<br>Randomized<br>Double-blind | Citalopram, 20 mg p.o. b.i.d. [titrated from 20 mg o.d. over 4 d] x 8 wks<br>Reboxetine, 4 mg p.o. b.i.d. [titrated from 4 mg o.d. over 4 d] x 8 wks | 35 | Citalopram had a moderate analgesic effect in patients with somatoform pain disorder; the effect did not correlate with changes in depressive scores | 19 |
| | Single-blind<br>Crossover<br>Placebo-controlled | Trazodone, 100 mg p.o.<br>Placebo | 11 | The acute administration of trazodone 100 mg partially mitigated the subjective and objective sleep and awakening quality changes associated with somatoform pain disorder | 20 |
| Hypochondriasis | Open | Paroxetine, up to 60 mg/d p.o. [dose adjusted acording to tolerability] x 12 wks | 11 | Paroxetine could be effective for the treatment of hypochondriasis. Controlled studies are warranted | 22 |
| | Open | Fluvoxamine, 150 mg p.o. b.i.d. [titrated from 50 mg/d over 6 wks] x 12 wks | 14 | Fluvoxamine was well tolerated and showed response rates of 72.7% after 6 weeks and 57.1% after 12 weeks of therapy (comparable to reported rates with fluoxetine), with significant improvements on self-reported and physician-administered hypochondriasis measures | 23 |
| | Open | Nefazodone, 300-600 mg/d p.o. [titrated from 50 mg b.i.d. over 3 wks] x 8 wks | 11 | Nefazodone showed efficacy for the treatment of hypochondriasis and could be a promising therapy for this condition | 24 |

*Continuation*

*Table I (cont.): Completed and ongoing studies of experimental therapies for somatoform disorders (continuously updated information available in Prous Science Integrity®).*

| Indication | Design | Treatments | n | Conclusions | Ref. |
|---|---|---|---|---|---|
| Hypochondriasis | Randomized | Cognitive-behavioral therapy x 6 sessions<br>Standard medical care | 187 | Individual and specifically designed cognitive-behavioral therapy showed significant long-term beneficial effects on hypochondriasis symptoms | 25 |
| | Comparative<br>Randomized<br>Single-blind | Cognitive-behavioral therapy x 16 over 6 mo<br>Psychodynamic psychotherapy | 80 | A phase II study studying the efficacy of cognitive-behavioral therapy compared with short-term psychodynamic psychotherapy for the treatment of hypochondriasis was completed | 26 |
| Body dysmorphic disorder | Pooled/meta-analysis | Cognitive-behavioral therapy<br>Clomipramine, Fluvoxamine, Fluoxetine or Citalopram | 314 | Both psychological and pharmacological therapies were effective for the treatment of body dysmorphic disorder, although cognitive-behavioral treatment could be the most useful | 33 |
| | Comparative<br>Randomized<br>Double-blind<br>Crossover | Clomipramine, 250 [max.] mg/d p.o. [titrated from 25 mg/d as tolerated] x 16 wks<br>Desipramine, 250 [max.] mg/d p.o. [titrated from 25 mg/d as tolerated] x 16 wks | 29 | Clomipramine was more effective than desipramine for the treatment of body dysmorphic disorder, being effective even in delusional patients | 34 |
| | Open | Fluvoxamine, 150 mg p.o. b.i.d. [titrated from 50 mg/d over 5 wks] x 16 wks | 30 | Fluvoxamine significantly improved delusionality in patients with body dysmorphic disorder. The degree of delusionality did not predict response to fluvoxamine | 35 |
| | Randomized<br>Double-blind<br>Placebo-controlled | Fluoxetine, 80 [max.] mg/d [titrated from 20 mg/d if tolerated] x 12 wks | 67 | Fluoxetine was more effective than placebo in patients with body dysmorphic disorder. Fluoxetine significantly improved impaired functioning (as measured by the LIFE-RIFT scale) and social and occupational functioning (according to the SOFAS scale), and it approached significant improvements on the mental health subscale of the SF-36 | 36, 37 |
| | Open | Citalopram, 20 mg/d p.o. x 2 wks → 40 mg/d p.o. x 2 wks → 60 mg/d p.o. x 8 wks | 15 | Citalopram was safe and effective for the treatment of body dysmorphic disorder, significantly improving psychosocial functioning and the quality of life | 38 |
| | Open | Escitalopram, 10 mg/d p.o. x 2 wks → 20 mg/d p.o. x 2 wks → 30 mg/d p.o. x 8 wks | 15 | Escitalopram was well tolerated and effective for the treatment of body dysmorphic disorder | 39 |
| | Multicenter<br>Randomized<br>Double-blind<br>Placebo-controlled | Escitalopram x 14 wks | 128 | A clinical trial was initiated to evaluate escitalopram for the treatment of body dysmorphic disorder and its efficacy for preventing relapse, as well as the effect on depressive and anxiety symptoms and on functioning and life satisfaction | 40 |
| | Randomized<br>Double-blind<br>Placebo-controlled | Pimozide, 10 mg/d [titrated from 2 mg/d if tolerated] + Fluoxetine, up to 80 mg/d p.o. x 8 wks<br>Placebo + Fluoxetine, up to 80 mg/d p.o. x 8 wks | 28 | Pimozide augmentation of fluoxetine therapy was not effective for the treatment of body dysmorphic disorder not responding to fluoxetine monotherapy, even in more delusional patients | 41 |
| | Randomized<br>Double-blind<br>Placebo-controlled | Olanzapine, 15 mg/d [titrated from 2.5 mg/d if tolerated] + Fluoxetine, 80 [max.] mg/d p.o. x 8 wks<br>Placebo + Fluoxetine, 80 [max.] mg/d p.o. x 8 wks | 6 | Olanzapine augmentation of fluoxetine therapy was not beneficial in patients with body dysmorphic disorder not responding to fluoxetine monotherapy | 42 |

*Continuation*

*Table I (cont.): Completed and ongoing studies of experimental therapies for somatoform disorders (continuously updated information available in Prous Science Integrity®).*

| Indication | Design | Treatments | n | Conclusions | Ref. |
|---|---|---|---|---|---|
| Body dysmorphic disorder | Comparative Randomized Double-blind | Cognitive-behavioral therapy + Serotonin reuptake inhibitor<br>Relaxation/stress management training + Serotonin reuptake inhibitor | 80 | A clinical study will investigate the efficacy of cognitive-behavioral therapy as an adjuvant to serotonin reuptake inhibitor therapy in patients with body dysmorphic disorder | 43 |
| | Open | Levetiracetam | 15 | A pilot trial was initiated to obtain data on levetiracetam monotherapy and levetiracetam augmentation of serotonin reuptake inhibitor therapy for the treatment of body dysmorphic disorder | 44 |
| | Multicenter Randomized Double-blind Placebo-controlled | Fluoxetine x 13 wks<br>Placebo | 37 | A clinical study was initiated to evaluate the efficacy and safety of fluoxetine for children and adolescents with body dysmorphic disorder | 45 |

with conversion disorder have identified approximately one-third of patients as having persistent active psychiatric problems, or having an episode of major depression at the time of follow-up (14). A brain-based "cognitive" model of conversion disorder has been developed based on imaging studies, which suggests a neuroscientific basis for the psychodynamic dissociation hypothesis (15).

The outcome of a series of patients with psychogenic movement disorder, a subtype of conversion disorder, has been reported. The disorder is characterized by movement symptoms such as tremor, dystonia, myoclonus, parkinsonism and gait disorders. Of 23 patients who were consecutively referred for outpatient psychiatric assessment, 15 agreed to be treated with antidepressants. Eighteen patients had at least one Axis 1 diagnosis and 3 had somatization disorder. Treated patients received citalopram or paroxetine for 8 weeks, and patients who did not respond after 4 weeks at an optimal dose were switched to treatment with venlafaxine. Of 10 treated patients with primary conversion disorder, 8 had marked motor and global improvements and 7 had complete remission. All of these patients had a current or previous depressive or anxiety disorder (16).

A randomized, double-blind, placebo-controlled study is currently ongoing to evaluate the efficacy of sertraline in patients with psychogenic nonepileptic seizures. The study aims to recruit 50 patients with psychogenic nonepileptic seizures and a co-morbid diagnosis of depression, anxiety or post-traumatic stress disorder (17).

## Pain disorder

In this disorder, pain is the predominant focus of the clinical presentation and is of sufficient severity to warrant clinical attention. Pain disorder is characterized according to the factors involved in the etiology and maintenance of the pain. Unemployment, disability and family problems frequently occur in individuals with chronic forms of pain disorder, and the lifetime course of the disorder may be complicated by substance dependence or abuse (mainly alcohol) in up to one-quarter of these individuals. Pain disorder is often associated with other mental disorders, especially mood and anxiety disorders. Sleep problems are also frequently associated with the disorder (1).

A preliminary open-label study evaluated the effects of moclobemide, a reversible monoamine oxidase (MAO) inhibitor, in 14 outpatients with somatoform pain disorder. Moclobemide was administered up to a maximum dose of 450 mg/day for 8 weeks. There were statistically significant improvements from baseline in total scores for pain, as assessed by a visual analogue scale (VAS). There were also statistically significant improvements in scores for depression, anxiety and sleeplessness (18).

A randomized, double-blind comparison of citalopram *versus* reboxetine was performed in 35 outpatients with pain disorder. All patients met selective criteria for pain disorder associated with psychological factors. Patients received citalopram 40 mg/day or reboxetine 8 mg/day for 8 weeks. Pain rating scores decreased significantly in the citalopram group, but not in the reboxetine group. There were no significant changes in depression scores in either group. The study provided some evidence for efficacy of a selective serotonin reuptake inhibitor (SSRI) in pain disorder; however, there was a high number of dropouts, which compromised the validity of the study (19).

The efficacy of trazodone, a triazolopyridine derivative with both antidepressant and antianxiety activity, was investigated in 11 patients with insomnia related to somatoform pain disorder. Using polysomnography and psychometry, acute administration of 100 mg of a controlled-release formulation of trazodone resulted in an increase in slow-wave sleep. There was also a reduction in the number of awakenings and stage shifts (20).

## Hypochondriasis

Hypochondriasis is a preoccupation with fears of having, or the idea that one has, a serious disease, based on

a misinterpretation of one or more bodily signs or symptoms. The preoccupation with bodily symptoms lasts for at least 6 months and may be related to minor physical abnormalities, vague and ambiguous physical sensations, as well as bodily functions. Individuals with hypochondriasis often have other mental disorders, particularly anxiety, depressive and other somatoform disorders. The prevalence of hypochondriasis in the general population has been estimated at between 1% and 5%, with a slightly higher prevalence among primary care outpatients (1).

No recent controlled studies of pharmacotherapy in hypochondriasis have been reported. This may be a consequence of the issues associated with its clear diagnostic separation from anxiety and depressive disorders (6). Researchers at the Mayo Clinic recently evaluated the conceptualization and treatment of hypochondriasis and concluded that this disorder most likely represented a form of obsessive-compulsive disorder. This conclusion was based on the overlapping functional properties of the two disorders (21). Three small open-label studies have provided some evidence for the efficacy of the SSRIs paroxetine and fluvoxamine, as well as for the antidepressant nefazodone, in hypochondriasis (22-24).

A randomized, controlled intervention study of cognitive-behavioral therapy in 187 patients with hypochondriasis was recently reported. In this study, patients were identified using a hypochondriasis questionnaire. Six sessions of individual cognitive-behavioral therapy resulted in statistically and clinically significant improvements in hypochondriac symptoms after 6 and 12 months compared with patients randomized to standard care. However, hypochondriac somatic symptoms were not significantly improved by treatment (25). Another study comparing cognitive-behavioral therapy with psychodynamic psychotherapy in patients with hypochondriasis has recently been completed in Denmark (26).

### Body dysmorphic disorder

Body dysmorphic disorder is a preoccupation with a defect in appearance. The defect is either imagined or, if a slight physical anomaly is present, the person's concern is markedly excessive. Complaints commonly involve imagined or slight flaws of the face or head, but any other body part may be the focus of concern. The preoccupation may simultaneously focus on several body parts. The prevalence of body dysmorphic disorder in cosmetic surgery and dermatology settings ranges from 6% to 15% (1). It is interesting to note that of all the somatoform disorders, body dysmorphic disorder was the only one that was not represented in the Dutch prevalence study (7). Body dysmorphic disorder may be associated with major depressive disorder, delusional disorder, social phobia and obsessive-compulsive disorder. In a prospective observational study, 39% of individuals with current body dysmorphic disorder had co-morbid lifetime social phobia, and 34% had current social phobia (27). In the same group of subjects, approximately one-third were classified as currently delusional and two-thirds as nondelusional according to the Brown Assessment of Beliefs Scale (BABS) (28). In addition, one-third of the subjects had a co-morbid lifetime eating disorder (29).

By far the largest body of recent research in the field of somatoform disorders relates to body dysmorphic disorder. However, this appears to be the result of a particular interest in the disorder by one group in Providence, Rhode Island, rather than a widespread interest in pharmacotherapeutic options for the treatment of the disorder. The Body Dysmorphic Disorder and Body Image Program is a specialty program affiliated with Butler Hospital and Brown Medical School (30). Such programs enable the conduct of research studies and will no doubt stimulate further understanding of and interest in the disorder.

A single-center, prospective, observational, longitudinal study of body dysmorphic disorder enrolled 200 subjects and resulted in improved understanding of predictors of remission, the relationship between body dysmorphic disorder and social phobia, co-morbidity of body dysmorphic disorder and eating disorders, and the clinical features and course of delusional *versus* nondelusional body dysmorphic disorder (27-29, 31, 32). Almost 50% of the subjects were referred by mental health professionals or nonpsychiatrist physicians, while the remainder were self-referred. The only exclusion criterion was the presence of an organic mental disorder. A total of 161 subjects met full DSM-IV-TR criteria for body dysmorphic disorder at the intake interview and also had 1 year of follow-up data. Individuals with a co-morbid personality disorder were less likely to achieve a full or partial remission from body dysmorphic disorder, but remission was not predicted by receipt of mental health treatment or non-mental health treatment, such as surgery or dermatological treatment, during the 1-year follow-up (31).

Both psychological and pharmacological therapies have been evaluated in the treatment of body dysmorphic disorder. Pharmacotherapy studies have focused primarily on SSRIs. A recent meta-analysis of studies published between 1994 and 2003 examined the efficacy of treatments for body dysmorphic disorder and compared the effectiveness of psychological and pharmacological therapies. The findings supported the effectiveness of both types of therapy, but indicated that cognitive-behavioral treatment may be the most useful (33).

A randomized, double-blind, crossover study compared the efficacy of clomipramine, an SSRI, with desipramine, a selective norepinephrine reuptake inhibitor (SNRI). A total of 29 patients were randomized to active treatment and received 8 weeks' treatment with each medication. A flexible dose-titration schedule was used, with a maximum dose of 250 mg/day or the highest tolerated dose for each medication. Clomipramine was significantly more effective than desipramine based on three clinician-rated primary outcome measures, including the Yale-Brown Obsessive Compulsive Scale (YBOCS) modified for body dysmorphic disorder. The superiority of clomipramine was independent of the pres-

ence of co-morbid diagnoses of obsessive-compulsive disorder, depression, social phobia or delusional beliefs (34).

The efficacy of fluvoxamine was evaluated in a prospective, open-label study in 30 subjects with body dysmorphic disorder. Fluvoxamine treatment was initiated at a dose of 50 mg/day and titrated to a maximum dose of 150 mg twice daily or the maximum tolerated dose for a total treatment period of 16 weeks. Nineteen (63%) subjects responded to treatment, as demonstrated by a decrease of at least 30% in YBOCS modified for body dysmorphic disorder. In this study, the presence of delusional beliefs did not predict for response (35).

A randomized, double-blind, placebo-controlled study evaluated the efficacy of fluoxetine in 67 patients with body dysmorphic disorder. Fluoxetine up to a maximum dose of 80 mg/day was administered for 12 weeks. Fluoxetine was significantly more effective than placebo as assessed by the YBOCS modified for body dysmorphic disorder, the primary outcome measure. The response rate was 53% in the fluoxetine group compared with 18% in the placebo group. Treatment response was independent of the duration and severity of the disorder, and the presence of major depression, obsessive-compulsive disorder or a personality disorder (36). Improvement in the symptoms and severity of body dysmorphic disorder was significantly correlated with improvement in functioning and quality of life (37).

A prospective, open-label study of citalopram was also conducted in 15 subjects who received citalopram up to 60 mg/day for 12 weeks. There was a significant improvement in YBOCS modified for body dysmorphic disorder, and 73% of subjects were responders. Psychosocial functioning also improved significantly (38). Very similar responses were observed in a prospective, open-label study of escitalopram administered at doses of up to 30 mg/day for 12 weeks (39). A randomized, double-blind, placebo-controlled relapse-prevention study of escitalopram is currently ongoing in patients with body dysmorphic disorder who respond to initial open-label treatment with escitalopram for 14 weeks. The primary outcome measure is the relapse of symptoms at month 6, and the anticipated enrollment is 128 subjects (40).

In addition to monotherapy intervention in body dysmorphic disorder, SSRI augmentation strategies have also been investigated to improve response to initial treatment. In a randomized, double-blind, placebo-controlled study in 28 subjects with an inadequate response to fluoxetine, augmentation with the antipsychotic pimozide for 8 weeks was no more effective than placebo augmentation (41). These results were consistent with a case series of 6 subjects who had an inadequate response to fluoxetine (mean dose of 70 mg/day) for at least 12 weeks. Of these, only 2 demonstrated minimal improvement following augmentation with the antipsychotic olanzapine (mean endpoint dose of 4.6 mg/day). The mean duration of olanzapine augmentation was 5.3 weeks. Of the 6 subjects, 2 experienced fatigue and 3 weight gain (42). A randomized, double-blind study is ongoing to evaluate the effectiveness of cognitive-behavioral therapy as an adjunct to therapeutic doses of SSRIs in up to 80 subjects (43).

Other ongoing studies in body dysmorphic disorder include an open-label study of the antiepileptic levetiracetam in up to 15 subjects (44) and a randomized, double-blind, placebo-controlled study of fluoxetine in pediatric body dysmorphic disorder (45).

The formal studies conducted in body dysmorphic disorder demonstrate the efficacy of SSRIs in this disorder. The pharmacotherapy received by individuals was assessed retrospectively in the longitudinal study described earlier (31, 32). Of the 200 subjects enrolled, 183 had met full DSM-IV-TR criteria for body dysmorphic disorder prior to entry and also had 1 year of follow-up data. Within this population, 59% reported receiving SSRIs. Among subjects who had taken psychotropic medication (78%), the mean number of medications received was five. However, only 30 (16%) subjects had at least one SSRI trial considered optimally adequate for the effective treatment of body dysmorphic disorder based on dose and duration of treatment. A further 21 (11%) subjects had a minimally adequate SSRI trial (32). A chart review of an additional 49 subjects showed that adequate trials of SSRIs led to a greater improvement in the symptoms of body dysmorphic disorder than inadequate trials (46). The same review also demonstrated that patients who discontinued an effective SSRI had an earlier time to relapse and higher relapse rate than patients who continued over 6 months of follow-up (47). Given the low percentage of subjects who received an adequate SSRI trial, the authors noted that the chronicity of body dysmorphic disorder in the longitudinal study was not surprising (48).

## Conclusions

This review highlights the lack of evidence to support pharmacotherapy in the treatment of somatoform disorders other than body dysmorphic disorder. Very few controlled studies have been performed, particularly in those disorders where most debate exists regarding their classification in DSM-IV-TR. The lack of recent studies may be a reflection of this debate, although the evaluation of therapies, particularly SSRIs, in body dysmorphic disorder suggests that the interest of one or two research groups can stimulate continued research and understanding of a particular disorder. Evidence indicates that SSRIs are effective in the treatment of body dysmorphic disorder, but many patients achieve a suboptimal response because they do not receive an adequate course of medication.

## References

1. *Somatoform disorders. In: American Psychiatric Association: Diagnostic and Statistical Manual of Mental Disorders, Fourth edition*. American Psychiatric Association Press, Washington, D.C., 2000, 485-511.

2. Janca, A. *Rethinking somatoform disorders*. Curr Opin Psychiatry 2005, 18(1): 65-71.

3. Mayou, R., Kirmayer, L.J., Simon, G., Kroenke, K., Sharpe, M. *Somatoform disorders: Time for a new approach in DSM-V*. Am J Psychiatry 2005, 162(5): 847-55.

4. Strassnig, M., Stowell, K.R., First, M.B., Pincus, H.A. *General medical and psychiatric perspectives on somatoform disorders: Separated by an uncommon language*. Curr Opin Psychiatry 2006, 19(2): 194-200.

5. Janca, A., Isaac, M., Ventouras, J. *Towards better understanding and management of somatoform disorders*. Int Rev Psychiatry 2006, 18(1): 5-12.

6. Creed, F., Barsky, A. *A systematic review of the epidemiology of somatisation disorder and hypochondriasis*. J Psychosomatic Res 2004, 56: 391-408.

7. De Waal, M.W., Arnold, I.A., Eekhof, J.A., Van Hemert, A.M. *Somatoform disorders in general practice*. Br J Psychiatry 2004, 184(6): 470-6.

8. WHO International Statistical Classification of Diseases and Related Health Problems, 10th Revision (ICD-10): http://www.who.int/classifications/icd/en/

9. Volz, H.P., Moller, H.J., Reimann, I., Stoll, K.-D. *Opipramol for the treatment of somatoform disorders results from a placebo-controlled trial*. Eur Neuropsychopharmacol 2000, 10(3): 211-7.

10. Volz, H.P., Murck, H., Kasper, S., Möller, H.-J. *St. John's wort extract (LI 160) in somatoform disorders: Results of a placebo-controlled trial*. Psychopharmacology (Berlin) 2002. 164(3): 294-300.

11. Rief, W., Hiller, W. *A new approach to the assessment of the treatment effects of somatoform disorders*. Psychosomatics 2003, 44(6): 492-8.

12. Müller, T., Mannel, M., Murck, H., Rahlfs, V.W. *Treatment of somatoform disorders with St. John's wort: A randomized, double blind and placebo-controlled trial*. Psychosom Med 2004, 66(4): 538-47.

13. Vaideanu, C., Nechifor, M., Boisteanu, P. *Amisulpride in the treatment of patients with somatoform disorders*. Eur Neuropsychopharmacol 2005, 15(Suppl. 2): Abst P2.003.

14. Hurwitz, T.A. *Somatization and conversion disorder*. Can J Psychiatry 2004, 49(3): 172-8.

15. Ballmeier, M., Schmidt, R. *Conversion disorder revisited*. Funct Neurol 2005, 20(3): 105-13.

16. Voon, V., Lang, A.E. *Antidepressant treatment outcomes of psychogenic movement disorder*. J Clin Psychiatry 2005, 66: 1529-34.

17. *Treatments for psychogenic nonepileptic seizures (NES) (NCT00159965)*. ClinicalTrials.gov Web site 2006.

18. Pirildar, S., Sezgin, U., Elbi, H., Uyar, M., Zileli, B. *A preliminary open-label study of moclobemide treatment of pain disorder*. Psychopharmacol Bull 2003, 37(3): 127-34.

19. Aragona, M., Bancheri, L., Perinelli, D., Tarsitani, L., Pizzimenti, A., Conte, A., Inghilleri, M. *Randomized double-blind comparison of serotonergic (citalopram) versus noradrenergic (reboxetine) reuptake inhibitors in outpatients with somatoform, DSM-IV-TR-TR pain disorder*. Eur J Pain 2005, 9(1): 33-8.

20. Saletu, B., Prause, W., Anderer, P., Mandi, M., Aigner, M., Mikova, O., Saletu-Zyhlarz, G.M. *Insomnia in somatoform pain disorder: Sleep laboratory studies on differences to controls and acute effects of trazodone, evaluated by the Somnolyzer 24 x 7 and the Siesta Database*. Neuropsychobiology 2005, 51(3): 148-63.

21. Abramowitz, J.S., Braddock, A.E. *Hypochondriasis: Conceptualization, treatment, and relationship to obsessive-compulsive disorder*. Psychiatr Clin N Am 2006, 29(2): 503-19.

22. Oosterbaan, D.B., Van Balkom, A.J.L.M., Van Boeijen, C.A., De Meij, J.G.J., Van Dyck, R. *An open study of paroxetine in hypochondriasis*. Prog Neuro-Psychopharmacol Biol Psychiatry 2001, 25(5): 1023-33.

23. Fallon, B.A., Qureshi, A.I., Schneier, F.R. et al. *An open trial of fluvoxamine for hypochondriasis*. Psychosomatics 2003, 44(4): 298-303.

24. Kjernisted, K.D., Enns, M.W., Lander, M. *An open-label clinical trial of nefazodone in hypochondriasis*. Psychosomatics 2002, 43(4): 290-4.

25. Barsky, A.J., Ahern, D.K. *Cognitive-behavior therapy for hypochondriasis: A randomized, controlled intervention trial*. 158th Annu Meet Am Psychiatr Assoc (May 21-26, Atlanta) 2005, Abst 47C.

26. *KATHY: Cognitive-behavioural therapy for hypochondriasis (NCT00208247)*. ClinicalTrials.gov Web site 2006.

27. Coles, M.E., Phillips, K.A., Menard, W. et al. *Body dysmorphic disorder and social phobia: Cross-sectional and prospective data*. Depress Anxiety 2006, 23(1): 26-33.

28. Phillips, K.A., Menard, W., Pagano, M.E., Fay, C., Stout, R.L. *Delusional versus nondelusional body dysmorphic disorder: Clinical features and course of illness*. J Psychiatr Res 2006, 40(2): 95-104.

29. Ruffolo, J.S., Phillips, K.A., Menard, W., Fay, C., Weisberg, R.B. *Comorbidity of body dysmorphic disorder and eating disorders: Severity of psychopathology and body image disturbance*. Int J Eat Disord 2006, 39(1): 11-9.

30. Body Image Program from Butler Hospital, Providence, Rhode Island: http://www.butler.org/body

31. Phillips, K.A., Pagano, M.E., Menard, W., Fay, C., Stout, R.L. *Predictors of remission from body dysmorphic disorder: A prospective study*. J Nerv Ment Dis 2005, 193(8): 564-7.

32. Phillips, K.A., Pagano, M.E., Menard, W.A., Stout, R.L. *A 12-month follow-up study of the course of body dysmorphic disorder*. Am J Psychiatry 2006; 163(5): 907-12.

33. Williams, J., Hadjistavropoulos, T., Sharpe, D. *A meta-analysis of psychological and pharmacological treatments for body dysmorphic disorder*. Behav Res Ther 2006, 44(1): 99-111.

34. Hollander, E., Allen, A., Kwon, J. et al. *Clomipramine vs desipramine crossover trial in body dysmorphic disorder*. Arch Gen Psychiatry 1999, 56(11): 1033-9.

35. Phillips, K.A., McElroy, S.L., Dwight, M.M., Eisen, J.L., Rasmussen, S.A. *Delusionality and response to open-label fluvoxamine in body dysmorphic disorder*. J Clin Psychiatry 2001, 62(2): 87-91.

36. Phillips, K.A., Albertini, R.S., Rasmussen, S.A. *A randomized placebo-controlled trial of fluoxetine in body dysmorphic disorder*. Arch Gen Psychiatry 2002, 59: 381-8.

37. Phillips, K.A., Rasmussen, S.A. *Change in psychosocial functioning and quality of life of patients with body dysmorphic disorder treated with fluoxetine: A placebo-controlled study*. Psychosomatics 2004, 45(5): 438-44.

38. Phillips, K.A., Najjar, F. *An open-label study of citalopram in body dysmorphic disorder*. J Clin Psychiatry 2003, 64(6): 715-20.

39. Phillips, K.A. *An open-label study of escitalopram in body dysmorphic disorder*. Int Clin Psychopharmacol 2006, 21(3): 177-9.

40. *Effectiveness of escitalopram in the treatment of body dysmorphic disorder (NCT00149799)*. ClinicalTrials.gov Web site 2006.

41. Phillips, K.A. *Placebo-controlled study of pimozide augmentation of fluoxetine in body dysmorphic disorder*. Am J Psychiatry 2005, 162(2): 377-9.

42. Phillips, K.A. *Olanzapine augmentation of fluoxetine in body dysmorphic disorder*. Am J Psychiatry 2005, 162(5): 1022-3.

43. *CBT as an adjunct to SRIs in the treatment of BDD (NCT00211809)*. ClinicalTrials.gov Web site 2006.

44. *Effectiveness of levetiracetam in the treatment of body dysmorphic disorder (NCT00265109)*. ClinicalTrials.gov Web site 2006.

45. *Fluoxetine in pediatric body dysmorphic disorder (NCT00246435)*. ClinicalTrials.gov Web site 2006.

46. Phillips, K.A., Pagano, M.E., Fay, C., Menard, W. *Pharmacotherapy received by individuals with body dysmorphic disorder*. 44th Annu NCDEU Meet (June 1-4, Phoenix) 2004, Abst 229.

47. Jain, S., Grant, J.E., Menard, W., Cerasoli, S., Phillips, K.A. *A chart-review study of SRI continuation treatment versus discontinuation in body dismorphic disorder*. 44th Annu New Clin Drug Eval Unit (NCDEU) Meet (June 1-4, Phoenix) 2004, Abst 231.

48. Phillips, K.A., Pagano, M.E., Menard, W.A., Fay, C., Stout, R.L. *A prospective longitudinal investigation of the course of body dysmorphic disorder (BDD) and pharmacotherapy received*. 45th Annu New Clin Drug Eval Unit (NCDEU) Meet (June 6-9, Boca Raton) 2005, Abst 81.