The Effects of SSRI’s on the Symptoms of OCD

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Acknowledgment

Acknowledgement for my participation in pursuit of my degree in counseling is owed to a random stranger on a flight from St. Louis to San Francisco. In our conversation, we were talking philosophically about relationships and she asked if I was a therapist. I told her I wasn’t but that I had plenty of experience in life that led me to understand the human psyche. From that moment, until I enrolled in my master’s program, I was in pursuit of a deeper grounding for my experience.

This paper topic was inspired by personal experience and those around me who manage feelings of anxiety, inadequacy and other shortcomings using the coping strategies associated with the diagnosis of Obsessive Compulsive Disorder, some with, and others without, the support of medications reviewed in this paper.

There are also numerous individuals who supported me emotionally while I took my journey to the completion of my degree. The most recent are my partner Chase Lindberger with whom I have become a better man. My first supporter would be my mom, Jamie S. Schmidt, a therapist herself without whom I would not be here and who to this day encourages me to practice the art of working with others who are on their journey to self-awareness and contentment. A big thanks to the both of them and everyone in between. Thank you.
Abstract

SSRI's are an effective pharmacological treatment strategy for treating symptoms of OCD. The benefit of treating OCD using SSRI’s was discovered as an unintended beneficial side effect from the treatment of depression using SSRI’s. While not everyone who experiences OCD symptoms benefit from SSRI’s, novel treatment approaches examining the augmentation of SSRI’s have been shown to provide additional benefits to those who remain resistant to the treatment of OCD using SSRI’s alone. Work remains to be done to understand the underlying neurological processes involved in OCD and to determine if there are more than one neurological pathway for the development of OCD symptoms. This work is necessary to develop more targeted, individualized and efficacious approaches to the treatment of OCD.
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The Effects of SSRI’s on the Symptoms of OCD

This literature review will examine the effects of selective serotonin reuptake inhibitors (SSRI’s) on the symptoms of obsessive-compulsive disorder (OCD). Characteristically, OCD consists of symptom clusters that include recurrent and intrusive thoughts, impulses or images that cause noticeable distress, as well as behaviors that are performed repetitively in response to these thoughts, impulses or images (American Psychiatric Association, 2000). OCD is frequently comorbid with other disorders including depression and other psychoses. The original efficacy for relief from symptoms of OCD was noted in clients who experienced relief from drugs originally intended to treat depression. Because there are several classes of drugs and several drugs within each class that are used to treat depression, many of these have been demonstrated to be effective in managing the symptoms of OCD. The antidepressants which have been demonstrated to have an effect on the symptoms of OCD include: tricyclic antidepressants (TCA’s), serotonin reuptake inhibitors (SRI’s), selective serotonin reuptake inhibitors (SSRI’s), and selective norepinephrine reuptake inhibitors (SNRI’s) a class of drugs that effects both serotonin and norepinephrine receptors.

A general discussion of the monoamine theory of mental illness and the various methods by which atypical antipsychotics, TCA’s, SRI’s, SSRI’s, and SNRI’s are thought to work will assist in understanding the rationale for the design of studies in this review. While the exact mechanism of each class and drug is unclear, all of these drugs’ lineage can be traced to research conducted in the 1950’s which gave rise to the monoamine theories.

Monoamine Theory of Mental Illness

In the 1950’s it was understood that dopamine transmission contributed in some way to numerous psychoses, including schizophrenia. In 1957, imipramine, the first TCA, was
discovered while searching for alternative antipsychotic medications to impact these dopamine transmitters. The original TCA’s were found to raise the effective concentrations of amines at the postsynaptic level. These drug discoveries gave birth to the monoamine theory of mental illness when coupled with the observation that reserpine, a drug designed to lower blood pressure, caused depression in patients taking the drug because it lowered monoamine levels. Further research has shown the primary monoamines found in humans are the catecholamines: dopamine, norepinephrine and epinephrine; and the indoleamine: serotonin (Cameron, 1999).

The current monoamine theory postulates that depression is due to a deficiency in one or a combination of the three monoamines: (a) serotonin; (b) noradrenaline (also known as norepinephrine); or (c) dopamine (Hackett, 1996). It has been postulated that monoamine involvement in brain disorders could occur in a variety of non-exclusive ways. The amount of the monoamine (serotonin, epinephrine, norepinephrine, and dopamine) is different in a person experiencing symptoms of depression than in a typical person in either an absolute sense or in terms of the amount available for use in transactions. Factors implicated in this theoretical construction of the theory include: (a) synthesis; (b) storage; (c) release; (d) reuptake; and (e) degradation of the metabolic pathways impacting the monoamines.

An additional explanatory theory postulates that the receptor system for the monoamines may be malfunctioning. This postulate implicates additional areas for possible explanation and sources of research for therapeutic intervention including quantity or functionality of one or all of the following: (a) postsynaptic receptors; (b) presynaptic autoreceptors; and (c) monoamine transport molecules (Cameron, 1999).

As the theory has evolved, researchers have attempted to achieve two results: (a) eliminate negative side effects by creating more specific drug agents; and (b) create more
efficacious agents by focusing on a subset of the presumed therapeutic mechanisms. Newer antidepressants such as fluoxetine, sertraline, and paroxetine demonstrate selectivity for inhibition of one substrate of serotonin (5-HT). While still others, such as venlafaxine, are thought to target more than one neurotransmitter and drugs such as mirtazapine are believed to act more directly on one of the other processes believed to underpin the final common pathway of antidepressant action (Hackett, 1996).

The monoamine theory continues to evolve as more information becomes available through research. Additional potential postulates to describe the effects seen include: (a) abnormalities in secondary messenger systems; (b) gene expression effects; (c) co-localization and release of other neurotransmitters from those sites previously identified; (d) monoamine systems modulatory effects on other neurotransmitter systems; and (e) interactions between hormones and neurotransmitter systems (Cameron, 1999).

**Atypical Antipsychotic Medication Mechanism**

In order to understand why some researchers have examined the effects of atypical antipsychotic medication it would be useful to understand their underlying mechanism. Atypical antipsychotic drugs have a blocking effect on D₂ dopamine receptors but seem to be more selective than the typical antipsychotic medications, targeting the intended pathway to a larger degree than the typical antipsychotic medications which are broad spectrum by definition. These atypical antipsychotic medications also block or partially block serotonin receptors (particularly 5HT₂ₐ,₃ and 5HT₁₆ receptors) like the SSRI’s. This combination of effects on both dopamine and serotonin receptors might be why atypical antipsychotic medications tend to have fewer side effects than typical antipsychotic medications.
The method in which this class of drugs works is unknown. However, research indicates that it is probable that they differ among the various drugs within the class. Indeed, it is known that the receptor binding profile of the atypical antipsychotic medications vary substantially between them. While it is presumed that modulation of the dopamine neurotransmitter system is necessary for all antipsychotic activity, the role of these medications on the serotonin systems of the brain is uncertain. It is believed by some that D₂ receptor antagonism, coupled with 5-HT₂A receptor antagonism (like the SSRI’s), is responsible for the activity profile of the class of atypical antipsychotic medications. While others believe that merely fast dissociation from the D₂ receptors allows for better transmission of the normal physiological dopamine surges, thus providing a better explanation of the evidence of how these medications create their effects ("Atypical"). Whatever the mechanism, this class of drugs unique profile, lower risk of side effects and presumed selectivity and partial blocking of the serotonin receptors has caused them to be the focus of augmentation therapies of the SSRI’s to treat the symptoms of OCD in those who are resistant to SSRI therapy only (Metin, Yazici, Tot, & Yazici, 2003).

Norepinephrine Reuptake Inhibitors (NRI’s) AKA Tricyclic Antidepressants (TCA)

Mechanism

Tricyclic antidepressants (TCA) are a class of antidepressant drugs first discovered and used in the 1950’s. The first TCA discovered was imipramine. This class of drugs is named after the drugs’ molecular structure, which contains three rings of atoms.

Most TCA’s are thought to work by inhibiting the re-uptake of the entire spectrum of neurotransmitters by nerve cells in the norepinephrine and serotonin families. For many years they were the first drug of choice for the treatment of depression. While they remain effective, they have been increasingly replaced by SSRI’s and other newer drugs because they are thought
to have fewer side effects due to SSRI’s selectivity ("Tricyclic"). However, some research is still focused on this class of drugs as a possible supplement to SSRI treatment resistant OCD (Barr, Goodman, Anand, McDougle, & Price, 1997).

**Serotonin Reuptake Inhibitors (SRI’s) and Selective Serotonin Reuptake Inhibitor (SSRI’s) Mechanism**

SRI’s and therefore, SSRI’s are a class of antidepressants. Essentially SSRI’s are thought to work the same way as SRI’s but on a more selective group of the serotonin neurotransmitters. Both SRI’s and SSRI’s are believed to act within the brain to increase the amount of the neurotransmitters available to complete communication between the transmitter and the receptor. SSRI’s specifically target serotonin (5-hydroxytryptamine or 5-HT), in the synaptic gap by inhibiting its re-uptake ("Selective Serotonin").

**Selective Norepinephrine Reuptake Inhibitors (SNRI’s)**

Serotonin norepinephrine reuptake inhibitors (SNRI’s) are a class of antidepressant used in the treatment of clinical depression and other affective disorders. They act upon two neurotransmitters in the brain that are known to play an important part in mood, namely, serotonin and norepinephrine. This can be contrasted with the SSRI’s, which act only on serotonin.

SNRI’s were developed more recently than SSRI’s, and therefore, there are fewer of them. Their efficacy as well as their tolerability appears to be somewhat better than the SSRI’s. While the specific cause of their increased efficacy and tolerability appears to be unknown, it is believed to be because of their compound or synergistic effect ("Serotonin"). They appear to have qualities of both the TCA’s and the SSRI’s. This has made them the subject of research to determine their efficacy in the treatment of OCD (Denys, van der Wee, van Megen, &
Westernberg, 2003), SSRI treatment resistant OCD (Hollander et al., 2003) and supplementation of SSRI’s to increase the time to achieve treatment results (Pallanti, Quercioli, & Bruscoli, 2004).

**The Effect of SSRI’s on Obsessive-Compulsive Disorder (OCD)**

**Relationship**

As set forth in Hollander et al. (2003) SRI’s and SSRI’s have been chosen as the first line of pharmacological intervention due to their demonstrated effectiveness for treating most individuals experiencing symptoms of OCD and low side effect profile. However, SSRI’s are not always effective for everyone in alleviating the symptoms of OCD. In fact, Hollander (2003) cites several studies which demonstrate that as many as 40% of individuals may not respond to these medications and in fact continue to exhibit significant symptoms of OCD even after taking a SRI or SSRI. Due to the strength of this relationship and the SRI’s/SSRI’s demonstrated general efficacy, the questions most researchers are attempting to discover are not whether they work but rather: proper dosing, (Bareggi et al., 2004); whether an individual SSRI is more effective than a TCA (Mundo, Rouillon, Figuera, & Stigler, 2001); whether SNRI’s are more effective than SSRI’s (Denys et al., 2003), (Hollander et al., 2003); clinical predictors of early response (Storch et al. 2006); are efficacious in children (Cheer & Figgitt, 2002), (Thomsen, Ebbesen, & Persson, 2001); are influenced by genetically identifiable variations of the patient (Uguz et al. 2009); or when co-administered with another agent are more efficacious than when administered singly (Barr et al., 1997), (Francobandiera, 2001), (Metin et al., 2003), (Pallanti & Bruscoli, 2004).
**Strength of the Relationship**

As discussed above, the relationship between SSRI’s and the reduction in symptoms associated with OCD are well known. However, there are a significant number of individuals for whom SSRI’s provide no relief. One of the questions that Bareggi (2004) and his team examined was whether the plasma level of the effective agent available within the blood stream of the participant was significant in the ability to predict whether an individual would respond. The results indicated that the level of medication available within the body was not indicative of whether an individual would respond. Those who did not respond were demonstrated to have as much metabolites of the agent in their blood as the responders. This apparent anomaly indicates that OCD may have multiple neurological pathways by which it may evince itself.

The hypothesis that multiple pathways may exist for impacting the symptoms of OCD has led to the introduction of other pharmacological agents as either synergistic agents (Barr et al., 1997), (Francobandiera, 2001), (Metin et al., 2003) and (Pallanti & Bruscoli, 2004) or those that contain selective but multiple targets (Denys et al., 2003) and (Hollander et al., 2003) in the use of SNRI’s. Hollander’s (2003) research sought out patients who had previously failed to respond to the SRI’s and introduced them to an SNRI, venlafaxine. In this study, even among those who had previously failed to respond to a SSRI, almost three quarters had a sustained reduction in OCD symptoms after having been introduced to venlafaxine.

**Evidence**

Evidence that is typically sited for purposes of determining that symptoms of OCD have been ameliorated includes the more general Clinical Global Improvement (CGI) (Guy, 1976) scale and the OCD specific Yale-Brown Obsessive Compulsive Scale (Y-BOCS) (Rosenfeld, Dar, Anderson, Kobak, & Greist, 1992). Sixty percent of the studies used the CGI to measure
overall improvement in participants’ symptoms. The scale ranges from 1 to 7. The scale is 1 = very much improved, 2 = much improved, 3 = minimally improved, 4 = no change, 5 = minimally worse, 6 = much worse, and 7 = very much worse. The amount of improvement necessary on the CGI to indicate general improvement necessary to rate a trial as a success varied from 3 and up (Bareggi et al., 2004), (Francobandiera, 2001), and (Mundo et al., 2001) to the more restrictive 2 and up (Cheer & Figgitt, 2002), (Hollander et al., 2003), and (Pallanti & Bruscoli, 2004). The CGI is a clinician’s judgment of an individual participant’s improvement from the beginning to the end of the trial.

Similarly, the more specific scale of the Y-BOCS or the Children Yale-Brown Obsessive Compulsive Scale (CY-BOCS) (Scahill et al., 1997) is used in twelve of the thirteen studies reviewed depending on the population measured. The Y-BOCS consists of five items measuring obsessive traits or symptoms and five items measuring compulsive traits or symptoms. These ten items are then scored from 0 to 4 with 0 indicating no symptoms or normal and 4 being most abnormal or extreme. The maximum combined score then is 40 and the lowest is 0. A typical number used as indicative of symptoms of OCD is 16 (Rosenfeld et al., 1992). Studies varied by the amount of change necessary to demonstrate improvement. One indicated the average change in points (Cheer & Figgitt, 2002), while others described in advance what was necessary to declare success (Bareggi et al., 2004) (25% change), (Denys et al., 2003) (50% change), and (Pallanti & Bruscoli, 2004) (35% change), while yet others examined the degree of change relative to their control group in an augmentation study (Pallanti & Bruscoli, 2004).

Using these measurements the results indicate that there is evidence for the effectiveness of SSRI’s in the treatment of the symptoms of OCD (Bareggi et al., 2004), (Cheer & Figgitt, 2002), (Mundo et al., 2001) and (Thomsen & Persson, 2001). Cheer’s research indicates that
when adolescents were treated with an SSRI for an extended period of time, they continued to demonstrate improvements for up to a year while receiving an SSRI treatment and that those who were in the control group who were switched to the SSRI once the trial was completed demonstrated a marked improvement in their CY-BOCS scores.

**SSRI’s Versus Tricyclic Antidepressants (TCA’s)**

Mundo et al. (2001) set out to determine whether the SSRI fluvoxamine was as effective as the tricyclic antidepressant clomipramine. In this study it was determined that the SSRI was as effective as the TCA and had fewer side effects. Two hundred and twenty-seven patients were randomized to take either the SSRI or the TCA. At the outset neither group differed in any significant manner in demographics or baseline clinical variables. Through the study twice as many participants withdrew due to side effects from the arm that included the TCA. During every measurement point in time there was no statistical difference between the two groups on any other measurement of clinical response. In this case Mundo et al. (2001) was capable of demonstrating that an SSRI had statistically identical efficacy as the TCA with fewer side effects.

**SSRI Versus SNRI**

Due to the numerous neurological pathways that potentially impact the symptoms of OCD, a number of studies have attempted to examine the effects of a newer class of drugs classified as SNRI’s which impact both the serotonin and norepinephrine receptors in the brain. Two studies were reviewed with differing conclusions.

The first study published by Hollander et al. (2003) was conducted in a long term retrospective study over a maximum of 56 months. This study indicated that there appeared to be a benefit to the usage of the SNRI, venlafaxine over SSRI’s. In this study, there was no
control for comorbidity, usage of other medications, or control for differing types of therapy. However, the researchers were able to demonstrate in their retrospective study that participants using venlafaxine had better results than those using SSRI’s.

However, under a shorter, more controlled trial, there were no benefits to venlafaxine over the SSRI, paroxetine (Denys et al., 2003). In this highly controlled (exclusion of comorbid diagnoses including depression) double blind study of twelve week duration there was no statistically significant difference in either the quality of response or the number of participants who responded to either venlafaxine (SNRI) or paroxetine (SSRI). The researchers concluded that while venlafaxine was effective with assisting in the resolution of symptoms of OCD, it was not more effective than the SSRI, paroxetine.

These two studies may not be in contradiction to one another for a variety of reasons. The first study lasted for a significantly longer period of time (up to 56 months) versus the shorter more controlled study (12 weeks). While the second study was highly controlled, the first allowed participants with any number of other comorbid presentations as well as additional medications to participate in the study. The study by Hollander et al. (2003) indicated that these very factors may have confounded the results that they noted.

**SSRI Alone Versus Augmented SSRI**

Four studies examined questions surrounding the augmentation of SSRI’s to determine if this combination was more efficacious than SSRI’s alone either in terms of latency or additional impact, (Barr et al., 1997), (Francobandiera, 2001), (Metin et al., 2003), and (Pallanti & Bruscoli, 2004). The results of these studies varied from no effect (Barr et al., 1997), to a reduction in time to achieve symptom reduction (Pallanti & Bruscoli, 2004), to assisting individuals who are otherwise non-responsive to SSRI’s alone (Francobandiera, 2001) and (Metin et al., 2003).
Pallanti and Bruscoli (2004) studied the effect of mirtazapine, a SNRI antidepressant that works on different neuroreceptors than the SSRI’s and had been shown in previous studies of depression to work more quickly than some of the SSRI’s. This study demonstrated that with mirtazapine there was in fact a quicker response for participants in reduction of their OCD symptoms. The typical response time (latency) for symptom reduction in individuals experiencing symptoms of OCD with only a SSRI is approximately eight weeks. The individuals in this study who were supplemented with mirtazapine experienced relief from their symptoms on average 50% faster, i.e. in four weeks. While there was a faster response there was no greater effect after the control group had been on the SSRI for eight weeks.

The studies by Francobandiera (2001) and Metin et al. (2003) demonstrated that with the addition of other specific psychopharmacological agents (atypical antipsychotic medications), that individuals who were previously unable to achieve relief from their symptoms of OCD on an SSRI only regime, responded favorably. Like the addition of mirtazapine, the agents selected were identified due to their ability to impact additional neuroreceptors thought to influence the exhibition of symptoms of OCD not merely due to their antipsychotic qualities.

**Methodology**

**Definitions**

The definition used to determine if participants were experiencing symptoms of OCD, and therefore eligible for medication trials, was based on the Diagnostic and Statistical Manual of the American Psychological Association. Four studies used the definition from the third edition revised (DSM III-R): (Barr et al., 1997), (Mundo et al., 2001), (Thomsen & Persson, 2001), and (Wagstaff, Cheer, Matheson, Ormrod, & Goa, 2002). Eight used the fourth edition: (Bareggi et al., 2004), (Denys et al., 2003), (Hollander et al., 2003), (Francobandiera, 2001),

(Pallanti & Bruscoli, 2004), (Storch et al. 2006), (Uguz et al. 2006) and (Van Nieuwerburgh et al. 2009). One used the fourth edition, text revision (DSM IV-TR); (Metin et al., 2003); and one provided no information for the basis of screening: (Cheer & Figgitt, 2002).

While the standard for measuring OCD changed over the course of the study from one version to the next, there are no substantive changes in the underlying diagnostic criteria

**Measurements**

There are generally well accepted standards for measuring the effects of medication on the symptoms of OCD. These include the Yale-Brown Obsessive Compulsive Disorder Scale (Y-BOCS) or the Children’s Yale-Brown Obsessive Compulsive Disorder Scale (CY-BOCS), the Clinical Global impression rating scale to determine if an intervention or medication trial has alleviated symptoms in a manner clinically significant and the Hamilton Depression (HAM-D) Rating Scale and Beck Depression Inventory (BDI) for examining the symptoms of major depression.

**Yale-Brown Obsessive Compulsive Disorder Scale (Y-BOCS) and the Children Yale-Brown Obsessive Compulsive Disorder Scale (CY-BOCS).** In 1989 Goodman and a team at the Yale University School of Medicine developed the Yale-Brown Obsessive Compulsive Scale and in 1992 a computerized version was developed (Rosenfeld et al., 1992). This tool assesses the severity of OCD symptoms independently of the type of obsessions and compulsions a patient may be exhibiting. The test has a high degree of agreement between raters with reports of intraclass correlations ranging from .88 to .98 (Rosenfeld et al., 1992). It has also shown a high rate of internal consistency ranging from .88 to .91 in the original research as well as having convergent validity with three other independent measurements of OCD with
coefficients ranging from .53 to .74 (Rosenfeld et al., 1992). As important, it also has been shown to be sensitive to measuring change over time.

An important caveat forwarded by Rosenfeld (1992) is that the human delivered Y-BOCS requires raters to be familiar with OCD. Rosenfeld noted that raters who were very familiar with OCD gave ratings different from those given by less experienced clinicians. The net result was that the reliability of the Y-BOCS could be compromised in multi-center studies where standardized measurement is essential. The computerized tests were found to be nearly as reliable as those administered by a professional clinician.

Rosenfeld (1992) noted that while the Y-BOCS was not intended to be used for diagnostic purposes, it has been adopted in numerous clinical settings involving drug studies where a score of 16 or above was used as a diagnostic determination of whether an individual was experiencing clinically significant symptoms of OCD.

The Children Yale-Brown Obsessive Compulsive Scale’s (CY-BOCS) reliability and validity results were published by Scahill et al. in 1997. In this report, the authors noted that the results of their tests demonstrated a high level of internal consistency, measuring 0.87 for the 10 items. The intraclass correlations for the CY-BOCS Total, Obsession, and Compulsion scores were 0.84, 0.91, and 0.66 respectively, suggesting a good to excellent interrater agreement for subscale and total scores. However, the authors noted that reliability and validity appear to be influenced by the subject’s age and cautioned that there were risks associated with the test when integrating data from parental and patient sources.

**Clinical Global Impression (CGI) of symptom severity and change rating.** The clinical global impression of symptom severity and change rating scale was initially introduced by Guy (1976) as editor in a publication produced by the National Institutes for Mental Health as
a compendium of assessment tools for psychopharmacology. It measures three items: (a) seriousness of the disease; (b) global improvement; and (c) pure drug effect. This is done by a clinician who is participating in the trial.

**Hamilton Depression (HAM-D) rating scale.** The Hamilton Depression (HAM-D) rating scale was originally developed and published by Hamilton in 1960. The HAM-D was developed as a measure of treatment outcome rather than a screening or diagnostic tool for depression (Hamilton, 1960). Although the HAM-D was not designed to diagnose depression, it is commonly used as a screening scale, particularly in the context of clinical trials to try to identify participants with depressive disorders. The HAM-D is a 21-item rating scaled used to systematize clinical observations of features related to depression. Ten items are ranked on a scale from 0 to 4; 9 items are ranked 0 to 2; and 2 items are ranked 0 to 3. Typically, a break score of 18-20 is used to differentiate persons with probable depressive disorder (Holroyd & Clayton, 2000). The HAM-D is completed by a trained observer after a 30-minute clinical interview that assesses symptoms of depression.

Problems noted with the HAM-D include a heterogeneous factor analytic structure; an emphasis on behavioral symptoms and somatic complaints that neglects self-reported feelings of distress; and an intermingling of frequency and intensity of symptoms in scoring (Holroyd & Clayton, 2000).

**Beck Depression Inventory (BDI).** The Beck Depression Inventory was originally published as a tool for measuring depression in 1961 (Beck, Ward, Mendelson, & Erbaugh). Over the years it has come under scrutiny when it has been used in populations that are using it as a self-reporting tool rather than as a clinician administered tool (Dahlstrom, Brooks, & Peterson, 1990). Dahlstrom’s team (1990) discovered that when the test was self-administered in
populations that are resistant to being assessed or interested in being assessed as depressed that the inventory and the questions progressive nature towards pathology create a rather simplistic method for a subject to guess how to skew the results by answering the items that appear later on the inventory to raise or lower their overall score. Therefore, it would be important to determine how this test was administered in any particular study in order to determine whether the results could be skewed by this phenomenon.

**Subjects**

Subjects in the studies ranged from children and adolescents and adults up to age seventy-eight.

**Children and adolescents.** Two studies focused on children and adolescents (Cheer & Figgitt, 2002) and (Thomsen & Persson, 2001), while one noted their inclusion (Hollander et al., 2003). Only the study by Cheer (2002) addressed the dosing issues present in child and adolescent psychopharmacological trials, namely what is a proper dose for a child?

**Comorbid diagnoses**

Because OCD, like many psychological disturbances, occurs in the presence of other disorders, it presents challenges to assess the efficacy of medical interventions on the symptoms of OCD alone. In order to isolate the effects of medication on symptoms of OCD a number of studies attempted to exclude completely from study, patients who had major depression or depressive symptoms (Bareggi et al., 2004), (Denys et al., 2003), (Pallanti & Bruscoli, 2004), (Storch et al. 2006) and (Van Nieuwerburgh et al. 2009) or allowed them to participate based upon the presence of depression as secondary to symptoms of OCD, i.e. OCD caused depressive symptoms (Mundo et al., 2001) and (Uguz et al. 2006). The remaining studies acknowledging that OCD occurs with other disorders either allowed anyone who did not have overt psychosis
SSRI's and OCD

(Francobandiera, 2001), (Metin et al., 2003) and (Thomsen & Persson, 2001) or allowed them to be on other medications (Hollander et al., 2003).

However, the variety of identified comorbid psychological diagnoses varied greatly in the studies that did not control for this factor. Hollander (2003) included a predominant number of participants who experienced mood disorders. In this study there were also a large number who experienced body dysmorphic disorder, social disorder and attention deficit disorder. Hollander’s experience from recruitment of subjects in this open study is reflective of the common additional diagnosis of some form of mood disorder with OCD.

**Drug Interactions**

Prior medication experience varied depending on the design study. Hollander (2003) allowed participants to be on any stable drug regime while others wanted either no medication for some time period prior to the start of the study (Denys et al., 2003), (Mundo et al., 2001) and (Thomsen & Persson, 2001) or only the presence of benzodiazepines (Bareggi et al., 2004) to assure that the other medications had cleared the participants body and would not confound the trial’s results. Pallanti (2004) sought only SRI naïve participants.

**Gaps in Existing Knowledge**

Gaps in knowledge exist primarily in two domains. First, what or which neurotransmitters and neuroreceptors are responsible for the creation of symptoms associated with OCD? Secondly and relatedly, are there variations in the type or kind of OCD based upon the variations that may exist in the number or variety of transmitters and receptors impacted, i.e. are individuals who experience symptoms associated with OCD impacted as a result of one, two or more sites, or combination of transmitter and receptor sites? Following this line of inquiry, while there are some individuals who experience symptoms of OCD separate and apart from
other diagnoses such as depression, there are not many. Are individuals who are experiencing symptoms of OCD separate and apart from other psychological phenomenon such as depression, Attention Deficit Disorder or body dysmorphia in some way different than those who do not, i.e. are they qualitatively different?

**Confounding Variables**

These basic gaps in knowledge are at the source of most of the confounding variables found throughout the studies. Many of the studies experienced confounding variables related to the presence of other psychological diagnoses or concomitant psychopharmacological agents. The challenge for researchers is that a well-designed trial controls for these variables by eliminating as many of the confounding variables as possible. However, without a clear understanding of the underlying causative agents of the symptoms of OCD and whether there are qualitatively different kinds of OCD, there is no clear method for determining whether the studies have confounding variables or not.

Hypothetically, it is desirable to study the effects of a single agent such as a SSRI or SNRI on individuals experiencing only the symptoms of OCD to determine whether it is efficacious or not. However, if the underlying disorder has more than one etiology, then what was previously classified as a confounding variable may in fact be a part of the underlying disorder and should be accounted for.

**Summary of Findings**

The research reviewed underscores the difficulties that both clinicians and individuals have when undertaking a determination of how best to pharmacologically treat symptoms of OCD. While it is possible to state that SSRI’s are beneficial in the treatment of the symptoms of OCD, they are not universally so, in fact, many individuals experience minimal or no relief from
the consumption of these agents. The dilemma for clinicians and researchers is that without a basic understanding of the underlying brain chemistry, both clinicians and the individuals experiencing OCD struggle to find treatment options appropriate for the individual, hoping that a combination can be found that is successful.

While research continues to be done to determine the etiology of the symptoms of OCD, unfortunately most of it is done on an ad hoc basis, formulated on the basis of expected benefits from existing drugs on presumed sites that may influence symptom expression. While progress continues to be made in the understanding of the causes of OCD in this manner, it is much like the early days of pharmacology where agents are applied to determine if there is a beneficial effect and based upon an understanding of how the drug is presumed to work, the underlying cause is declared to fit the model. While this approach may have some merit using agents that are presumed to impact a single neurotransmitter/receptor site like the SSRI’s, it fails miserably in the unknown synergistic effects of SNRI’s, and SSRI’s and antipsychotic medications. These synergistic effects have in fact been the source of evolution for the underlying theory supporting the monoamine theory for mood regulation upon which the SSRI’s were based in the first place.

**Conclusions**

**Clinician’s Usage**

This review provides mixed evidence of the efficacy of medication in the treatment of symptoms of OCD. Enough patients with and without comorbid diagnosis and confounding variables appear to achieve relief from symptoms associated with OCD when taking medication that a clinician should not dismiss out of hand a client’s request or the potential to explore relief using these pharmacological agents. However, this review does not suggest that there is one treatment option or pharmacological agent(s) that are superior or even effective in all
circumstances to warrant it as a first line of treatment in the absence of a client’s request or pernicious symptomology that resists other more traditional treatment options available to the clinician in the absence of medical intervention.

SSRI’s remain an effective agent for the treatment of the symptoms of OCD. However, as our knowledge of OCD and the underlying neurological causes of behavior evolve we are likely to develop more effective, targeted and individualized treatment options. It is likely that the usage of SSRI’s will be looked back upon as a quaint yet barbaric method for addressing the causes of OCD as our knowledge progresses. In the meantime, they are one of the best pharmacological treatment strategies that exist today due to their efficacy and low side effect profile.

**Recommendations for Future Research**

The best research that exists is that which studies the effects of an individual agent on an individual variable. Unfortunately in the study of OCD the underlying causative agent or source of dysfunction at the neurological level is not as well understood as would be desirable for the creation of pharmacological therapeutic interventions. This fact is reflected in the very method by which these classes of drugs have been found to have an effect on the symptoms of OCD at all, i.e. as a beneficial side effect to the treatment of depression. Basic research to understand the neurotransmitters and receptors involved in the generation of symptoms consistent with OCD would be highly useful. This might be achieved by the usage of radiologically activated medications to determine where or how they are absorbed, used or otherwise create their impact on brain chemistry.

This research might also be used to determine whether there are different types of OCD which respond better to one or a combination of medications. It could also help explain why
some individuals respond successfully to SSRI’s alone while others respond only when supplemented by another medication that is presumed to effect another set of neuroreceptors.
References


