

Pediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcal
Infections (PANDAS):
Problems in Diagnosis, Explanation and Treatment

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May 2017

I would like to thank my three readers: Dr. Sasha Fleary, Dr. Kyle Williams, and Dr. George Scarlett. As my primary reader, Dr. Fleary worked very closely with me and guided me throughout the whole process. I cannot thank Dr. Fleary enough for advising me, allowing me to learn so much about research over the course of the year. Another special thank you to Dr. Williams, who works in the PANDAS field, for helping me find pertinent studies that aided in guiding and organizing my thesis as a whole. In addition, thank you to my family and everyone who supported me through this year, it has been an incredible experience!

My Story and Passion

When I was seven-years old, my older brother and I went off to summer camp together. This should have been the time of my life: bunking with friends, playing sports all day, and just hanging out. I was well-adjusted and on my way to a care-free and great first experience. Three weeks into the summer I contracted a Streptococcal infection. It should not have been a cataclysmic event, as blood tests and antibiotics normally manage this well. But, it triggered an unusual autoimmune response known as Pediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcal Infections (PANDAS).

I did not know what it was or realize at the time what was going on, but looking back I remember it all vividly. Before the infection I was a typical normal little boy, but suddenly, everything began to feel different. There was an “overnight” change; I had developed severe symptoms of Obsessive Compulsive Disorder (OCD), anxiety, tics and cognitive challenges. This abrupt transformation was triggered by exposure to and development of a Streptococcal infection, leading to a high streptococcal antibody titer in my blood.

The condition persisted for several years. Through cognitive behavior therapy and supportive help from my parents, many of the deficits were mitigated. While I am still mildly affected, I have used this stumbling block to make me stronger. I used PANDAS and my experiences to fuel my work ethic and my passion.

It was not until the middle of high school, when I first learned what this disorder actually was and that I had it. With a gentle and thorough explanation, my parents shared the original twenty-page report completed by my doctor at the time. While reading it and

beginning to process this news, I was taken back to the original onset of my symptoms. I found myself remembering the tics, the OCD and my unusual behaviors as a child. I knew I wanted to learn more, research more, and find a way to help other children and families affected by PANDAS.

I am following through on that goal now, with this thesis and my pursuit of further research on this diagnosis.

The Proposal and Research Questions

My proposal begins with a discussion of research questions that I used to guide the literature review performed for this thesis. My experiences with PANDAS have left me with unanswered questions that I will pursue in this proposal:

- 1) What is PANDAS? How is it diagnosed and treated?
- 2) What is the difference between PANDAS and OCD?
- 3) How can family systems theory explain the interrelationship between children with PANDAS and their family?
- 4) With an understanding of family systems theory, how does the family impact OCD treatment? What lessons can be learned specifically for PANDAS?

Controversy exists between PANDAS and OCD: PANDAS can be misdiagnosed for OCD and vice versa. The PANDAS field is much younger than that of OCD; information on the pathogenesis and family impact is much more extensive in OCD. This information, however, is useful to the PANDAS field because the two disorders share key characteristics.

By investigating the role of the family through the lens of Family Systems Theory, I will investigate, speculate, and propose future research opportunities on family impact and family accommodation differences in PANDAS as compared to OCD. I hope to expand the PANDAS field by learning more about the role of the family to help families and children who are diagnosed with PANDAS.

Literature Review

1) What is PANDAS? How is it diagnosed and treated?

Overview. Since it was first described nearly two decades ago, Pediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcal Infections (PANDAS) has perplexed researchers seeking to understand its pathways. PANDAS was first described by Swedo et al., (1998) using five criteria: 1) onset of Obsessive-Compulsive Disorder (OCD) and/or Tic disorder; 2) prepubertal onset of symptoms; 3) episodic course of symptom severity; 4) correlation with Streptococcal infections; and 5) neurological abnormalities. As a prominent PANDAS symptom, OCD plays a major role in the discussion of PANDAS because of their many similarities. OCD, as an anxiety disorder, has two major components: the presence of undesired thoughts and ideas that lead to anxiety and obsessions; and the use of rituals to attempt to minimize stress in the short term due to the compulsions (Abrahamowitz, Whiteside, & Deacon, 2006).

Based on their own research in 2015, the PANDAS Network (created to advance the PANDAS field) made a “conservative estimate” that one in two hundred children in the U.S.A have PANDAS. Dr. Susan Swedo was quoted as saying “these (PANDAS) kids may make up as much as twenty-five percent of children diagnosed with OCD, as well as Tic disorders such as Tourette Syndrome” (Westly, 2010, p. 17). Dr. Swedo

explains that because the disorder is newly described, PANDAS may be misdiagnosed as another disorder. National statistics on the demographic breakdown of PANDAS diagnosis is unavailable. However, one study (Calaprice, Tona, Parker-Athill, & Murphy, 2017) performed demographic analysis on 698 patients with a clinical diagnosis of PANDAS and found differing demographic characteristics for males and females. Specifically, 64% of the sample was male, and for males the mean age was 11.4 years old, 59% had prepubertal onset, 32% had onset during puberty, and the mean age of onset was 7.1 years old. On the other hand, 34% of the sample was female, and for females the mean age was 12.4 years old, 39% had prepubertal onset, 34% had onset during puberty, and the mean age of onset was 8.1 years old. In this study, 2% did not report their sex. At older ages of onset of PANDAS, gender distribution becomes nearly even, but for younger children the PANDAS population is heavily skewed towards males (Calaprice et al., 2017). Prior infection was found in 65% of patients and 54% specifically reported a Streptococcal infection, demonstrating that for most PANDAS diagnoses there was an infection that possibly triggered the onset of the disorder.

When the history of infection and the pace of onset are not considered, the symptoms of PANDAS and OCD are practically indistinguishable. However, if onset (sudden vs. gradual) and history of recent infection (like Streptococcal infection) are taken into account, the two disorders begin to show their unique characteristics.

Status of Research on PANDAS – Controversial, Inconclusive and Divided.

Much about PANDAS is still uncertain and inconclusive. Distinguishing between PANDAS and OCD on the basis of treatment and therapy or pathogenesis, is widely debated and controversial, especially because PANDAS is so recently described.

Currently, treatment for PANDAS is accomplished through cognitive behavior therapy, family counseling, and habit reversal (Esposito, Bianchini, Baggi, Fattizzo, & Rigante, 2014; Walsh & McDougle, 2001). When treating PANDAS, physicians treat the symptoms (e.g., OCD, tics, and neurological abnormalities) separately rather than treating the condition as a whole. As mentioned, OCD, one of the primary symptoms of PANDAS, is described as anxiety due to obsessions, like impulses, or actions beyond control (Gabby et al., 2008). Specific to OCD, the treatment options include cognitive behavioral therapy using exposure and response prevention, and pharmacological treatment, specifically a selective serotonin re-uptake inhibitor (Luo, 2004). An application of Cognitive Behavioral Therapy is mindfulness, where there is a building of awareness and acceptance of compulsions and unwanted thoughts instead of eliminating the compulsions (OCD Center of Los Angeles, n.d.). In this application, the acceptance of these compulsions is the first step in attempting to reduce the OCD symptom severity (OCD Center of Los Angeles, n.d.). Tic Disorders, another prominent PANDAS symptom, are recognized in people who display involuntary motor movements like blinking or head jerks worsened by stress (Gabby et al., 2008). Tic Disorders like Tourette's Syndrome are treated using α -adrenergic agonists, typical and atypical neuroleptic agents like haloperidol, pimozide and risperidone (Gabby et al., 2008). Other possible treatments for PANDAS symptoms include: adeno-tonsillectomy, antibiotic therapy, intravenous immunoglobulin, and cognitive behavioral therapy (Farhood et al., 2016). The basis of the use of adeno-tonsillectomy, antibiotic therapy, and intravenous immunoglobulin as treatment options is these in one way or another protect against recurrent infections like Streptococcus and attempt to lower Streptococcal blood titers.

Orvidas and Slattery (2001) conducted research on two siblings who displayed PANDAS symptoms during a Streptococcal infection. These two affected children underwent tonsillectomies; the results showed that after an eleven month postoperative time period, one child showed significant improvements and the other had a complete resolution of symptoms. Another sibling study included one child with Tourette's Syndrome and one with OCD; both showed great improvements after adeno-tonsillectomy (Heubi & Shott, 2003). However, not all studies show such positive results (Murphy, Lewin, Parker-Athill, Storch, & Mutch, 2013; Pavone et al., 2014). Murphy et al. (2013) looked at two groups of PANDAS patients where approximately half had adeno-tonsillectomies. Interestingly, these two groups showed no significant differences in streptococcal titer levels and no significant differences in the severity of symptoms (Murphy et al., 2013). Pavone et al. (2014) took a similar approach to their research and again the two groups showed no difference in symptom severity or titer levels. Tonsillectomy with or without adenoidectomy is a treatment option for children with PANDAS due to the link to prior Streptococcal infection, but the benefits are inconsistent.

Antibiotic therapy, used to alleviate Streptococcal infections, appears to be just as inconclusive, where some studies show an alleviation of symptoms while others demonstrate no significant difference between the placebo and treatment groups. In one double-blind, randomized, controlled study, one group received a placebo while the other oral penicillin (Streptococcal infections are typically sensitive to penicillin antibiotics); the results show no significant difference in symptom severity between the two groups (Garvey et al., 1999). On the other hand, Murphy and Pichichero (2002) administered

antibiotics to treat Streptococcal infection and related neuropsychiatric symptoms, and the results of this study showed improvement in symptom severity. These findings are contradictory. Antibiotic use is known to treat Streptococcal infections, as well as other types of Streptococcus, but it is still unknown whether this treatment is effective in alleviating PANDAS symptoms when attempting to alleviate Streptococcal infections.

The field of PANDAS research in children is divided and many studies are either statistically insignificant or contradictory. In an attempt to separate OCD and tics from PANDAS, studies have focused on identifying features that differentiate the two, but the findings have not been conclusive (Macerollo & Martino, 2013). There has also been an effort to identify biomarkers to support the diagnosis of certain conditions, but none has been able to separate PANDAS from OCD (Esposito, 2014). Without more conclusive evidence to differentiate PANDAS, these diagnostic challenges will continue for physicians and their patients.

Currently, the connection between the onset of PANDAS symptoms and Streptococcal infection remains in dispute. The uncertainty has been created by the lack of definitive data to support a causal relationship, despite a plethora of existing literature on this topic. Some studies found no relationship between Streptococcal infections (and the resulting inflammation) and neuropsychiatric syndromes like PANDAS (Schrag et al., 2009; Perrin et al., 2004; Teixeira, Rodrigues, Marques, Miguel, & Fontenelle, 2014). After looking at a database of patients with OCD, Tourette Syndrome, and tics, Schrag et al. (2009) concluded that there is no increased risk of PANDAS symptoms with prior Streptococcal infections. The same study concluded there is no significant relationship between the onset of symptoms and previous Streptococcal infection, but there may be a

weak association with Streptococcal infections and OCD (Schrag et al., 2009). Several studies strongly support a relationship between neuropsychiatric disorders and Streptococcal infections (Murphy, Storch, Lewin, Edge, & Goodman, 2012; Lin, 2010; Mell, Davis, & Owens, 2005). Murphy et al. (2012) found that children who were diagnosed with PANDAS had an increased rate of tonsillectomy/adenoidectomy, which indicates a higher rate of infections like Streptococcus. Based on this criterion, Murphy et al. (2012) concluded that the sudden onset of OCD and/or tics is associated with previous Streptococcal infections. A potential flaw in the Schrag et al. (2009) study is that the researchers looked at patients from the age of 2-25 years old; this age range is problematic since the onset of PANDAS is prepubescent (Swedo et al., 1998). The expanded age range could explain why the association between infection and symptoms were statistically insignificant.

In further support of the connection between PANDAS symptoms and prior onset of Streptococcal infection, one study (Perez-Vigil, Cruz, Brander, Isomura, Gromark, & Mataix-Cols, 2016) analyzed 74 reports, examined the association between autoimmune diseases and OCD/Tic Disorders, and found “modest evidence” for the association and causal relationship of Streptococcal infections triggering PANDAS (Perez-Vigil et al., 2016). This study supports a relationship between Streptococcal infections and the sudden onset of symptoms in PANDAS as results show the onset of symptoms is often immediately preceded by a Streptococcal infection.

The data on the pathogenesis of PANDAS is also inconclusive. The theories for pathogenesis include: triggers due to infection, neurophysiological aberrations, regional brain dysfunction, reactivity between infectious agents and the central nervous system,

and possible genetic susceptibility (Swedo, 1998; Gabby 2008). One of the better-studied theories of pathogenesis is that Streptococcal infection may lead to PANDAS symptoms. The mechanism in this theory supports the concept that infection causes creation of anti-Streptococcal antibodies; these antibodies produce an autoimmune response via “molecular mimicry” in the basal ganglia of the brain; the basal ganglia of the brain control behavior and movement (Garvey, Giedd, & Swedo, 1998). Differing slightly in their infectious and autoimmune etiology, many studies support the same conclusion that the pathogenesis is post-infectious autoimmunity or just post-infectious, which means that the possible pathogenesis begins with a prior infection leading to PANDAS (Swedo et al., 1998; Garvey et al., 1998; Mell et al., 2005; Falcini, Lepri, Rigante, Bertini, & Cerinic, 2013). The Swedo et al. (1998) study found that Streptococcal infections triggered an exacerbation of symptoms. The same study (Swedo et al., 1998) demonstrated support for a pathogenic mechanism of PANDAS; a pathogen like Streptococcus is introduced to a susceptible host that leads to an immune response, which evolves into PANDAS or Sydenham’s Chorea. These investigators also believe that PANDAS is linked to infection through a type of molecular mimicry effecting either basal ganglia or the central nervous system.

The studies that support the association and causal relationship between the onset of symptoms and prior infection also comment on some possible risk factors for PANDAS. One risk factor shows that males are at a greater risk of developing PANDAS (Swedo et al., 1990; Falcini et al., 2013). In the Swedo et al. study (1998), approximately seventy-five percent of children with PANDAS were male. There is an increased risk of PANDAS during the prepubertal years (6±2 years), possibly because of the increased

chance of a Streptococcal infection during those same years (Swedo et al., 1998; Falcini et al., 2013). Family factors, like genetics and autoimmune infection history, may also play a role in risk for PANDAS, pointing to the possibility that there is an autosomal recessive vulnerability trait that gives PANDAS a genetic predisposition (Swedo et al., 1998). These risk factors are important in making a diagnosis because it can help predict children who are at risk of developing PANDAS and can increase confidence in diagnosis of PANDAS.

In the short time since PANDAS has been described, the PANDAS field has learned much about this interesting yet mysterious disorder. The medical community is still puzzled by many of the mechanisms of PANDAS and the pathophysiology of the disorder. Many pieces of the PANDAS puzzle remain inconclusive, inconsistent, or lack statistically significant results. One critical question remains: is there a relationship between PANDAS symptoms and Streptococcal infections, and will increased research on this prove a distinction between PANDAS and OCD? If a connection can be confirmed, doctors can more confidently diagnose PANDAS, which will lead to better treatment and patient care.

2) *What is the difference between PANDAS and OCD?*

PANDAS vs. OCD. This is a challenging question that is currently being studied because the two disorders are so similar. The American Psychiatric Association (2000) describes OCD as recurrent and persistent obsessions and/or compulsions that are time consuming or cause distress or impairment of functioning. OCD is also described as the presence of undesirable thoughts that lead to anxiety and stress, which leads to the use of rituals to attempt to reduce distress (Abrahamowitz, Whiteside, & Deacon, 2006). The

alleviation of stress with the use of rituals is generally short term. Impacting 1-3% of all children (Karno et al., 1988; Ruscio et al., 2010), OCD is caused by both genetic and environmental factors (Geller & March, 2012; Koran & Simpson, 2013; Stewart & Pauls, 2010; Pauls, 2008). OCD burdens the family (Grover & Dutt, 2011; Ramos-Cerquiera et al., 2008; Steketee, 1997; Stengler-Wenzke et al., 2004) and the child is impacted by the family as seen in cases of family accommodation (Albert et al., 2010; Lebowitz, Panza, Su, & Bloch, 2012). Family accommodation is present when a family member, generally the parents, facilitates symptoms by allowing symptoms of rituals to continue (Calvocoressi et al., 1995). A parent might allow their child with OCD to turn the light switch on and off fifty times to reduce stress short term, but this has been seen to facilitate and exacerbate OCD symptoms. OCD is a neurological disorder with several possible etiologies, including inherited genetic polymorphisms (Nicolini, Arnold, Nestadt, Lanzagorta, & Kennedy, 2009), where rates of OCD are shown to be significantly higher in relatives. Although the field is inconclusive, the leading pathogenic hypothesis for PANDAS is the onset of OCD and/or tics is associated with prior Group A streptococcal infection (Swedo et al., 1998).

Critics of the separation of PANDAS from OCD argue there is no consensus on a pathogenic mechanism, and with this lack of consensus, there are no clear clinical characteristics or biomarkers that differentiate PANDAS from OCD or Tic Disorders (Perrin et al., 2004). However, possible biomarkers may be identified in the basal ganglia. Murphy and Pichichero (2002) and Elia et al. (2005) showed there may be additional symptoms involved in PANDAS beyond those described by Swedo et al. (1998), including urinary urgency, impulsivity, acute deterioration in handwriting and

separation anxiety (Murphy & Pichichero, 2002; Elia et al., 2005). Urinary urgency and handwriting deterioration could be connected to PANDAS as they are regulated through the basal ganglia, (Capone, Pilato, Profice, Pravata, & Di Lazzaro, 2009; Yamamoto et al., 2009) lending more evidence that the basal ganglia may contain biomarkers for PANDAS. Basal ganglia have been seen to play a role in the micturition reflex (involved in control of urination) in animals (Dalmose, Bjarkam, Sørensen, Djurhuus, & Jørgensen, 2004) and humans (Seif et al., 2004). Urinary urgency and deterioration in handwriting has recently been seen as an associated symptom of PANDAS, which may indicate that the basal ganglia, also related to these two symptoms, is a biomarker for PANDAS. In further support of unique biomarkers, several studies found a correlation between anti-Streptococcal antibody titer levels, basal ganglia volumes, and elevated anti-neuronal antibodies in children with PANDAS (Peterson et al., 2000; Singer et al., 2004; Dale, Heyman, Giovannoni, & Church, 2005).

One study used six instruments to examine the differences between OCD and PANDAS (Bernstein, Victor, Pipal, & Williams, 2010). Bernstein et al. (2010) measured anxiety, severity of obsessions/compulsions, the presence of tics, to describe the characteristics of symptoms, to obtain medical history, and to measure cognitive function. This study found interesting similarities and differences between the two disorders. Bernstein et al. (2010) found no significant difference in mean age of the children, socioeconomic status, mean IQ and OCD severity, suggesting that the groups were similar. Though not statistically significant, the same study found interesting trends including higher tic severity, higher Antistreptolysin O (ASO) titer levels, and higher antiDNase B titer levels in PANDAS groups. Based on parent-completed questionnaires,

Bernstein et al., (2010) found that children with PANDAS were significantly more likely to have separation anxiety, urinary urgency, oppositional defiant behavior, mood swings, inattention, hyperactivity, impulsivity, abnormal hand or finger movements, and decline in handwriting than children with OCD. This study showed that children diagnosed with PANDAS and children diagnosed with OCD may have different symptomatology despite the many similarities the two disorders share in their classic symptoms like anxiety and obsessions.

3) How can family systems theory explain the interrelationship between a child with PANDAS and his or her family?

Family Systems Theory. Several researchers have contributed to family systems theory. I will focus on models presented by Bowen as well as Minuchin. Both sets of researchers believe that individuals should be studied within the context of their family. Family members are deeply connected emotionally and this complexity establishes the basis of this theory. The Family Systems Theory, rooted in evolutionary theory, demonstrates the family's interdependence and gives perspective on how an individual uses knowledge about the family and how each family member impacts each other.

Framing and Reframing. In looking at the family system, the concept of framing and reframing is an important one, especially in therapy. In framing and reframing, as described by Minuchin and Fishman (1981), the family can look at the situation through a new perspective, which can increase the differentiation of the family as a whole allowing the family to better cope with the situation. The idea behind framing and reframing is that through therapy the issues can be presented in a new way. Piacentini et al. (2007) gives an example of reframing in OCD: "That's just my OCD talking and, if I check the

lock, my OCD will become more powerful and win” (p. 47). This is a great way to reframe an OCD compulsion because it puts the power and control back into the individual and allows the person to fight back and not allow the compulsions to take over. Framing and reframing is a powerful technique in therapy both for the family and the patient as it can change perspectives to a more beneficial and therapeutic way, not by changing what they believe in, but by reframing the lens the patient and family looks through.

Bowen’s Family Systems Theory. This is a trans-generational approach that shows emotional patterns in families as they continue in similar ways through each generation. Bowen’s Family Systems Theory, has eight broad concepts presented in hierarchical order: triangles, differentiation of self, nuclear family emotional system, family projection process, multigenerational transmission process, emotional cutoff, sibling position, and societal emotional process. In reviewing the concepts of Family Systems Theory, it is important to note that the examples that relate the concept to PANDAS are hypothetical scenarios used to illustrate the impact of the family through a Family Systems Theory lens.

Triangles. The concept of triangles looks at relationships and the tension between them. The triangle represents a three-person relationship system, and is the first ingredient to larger emotional systems because the triangle relationship is considered the smallest stable relationship (Kerr, 2000). With interspersed stress, a three-person system is more stable than a two-person system, and in periods of high stress, can “interlock” with other triangle systems to increase stability (Kerr, 2000). Fogarty (1976) described how people want to be close and in relationships. People handle stress and anxiety by

forming groups of three, or a triangle. Kerr (2000) argued that in tranquil periods there is a fear and anxiety of being the “odd man out”. Two are insiders and strengthen their bond by choosing each other and one is an outsider who attempts to become an insider as he or she is in distress. As tensions increase, the relatively more uncomfortable insider will try to become closer with the outsider, changing the relationships and functioning within the triangle. Finally, in high-tension situations, the outsider becomes the desirable member, while the insiders fight with each other. The insider might attempt to become an outsider by provoking the outsider to fight with the other insider. These interactions are common in everyday life. Movement of position from insider to outsider is important in understanding triangles because it can impact clinical problems and elicit depression or even physical illness (Kerr, 2000). This central concept to family systems theory is relevant to families where a child is diagnosed with PANDAS because it evaluates tension, stress, and anxiety (an integral symptom in PANDAS). Triangles can take different forms, one of which can be with siblings. In a family with three children the siblings can form a triangle relationship that follows the description of Family Systems Theory. For example, two of the three children are close with each other and the third child is the outsider. The bond between the first two strengthens whereas stress rises in the third child as he or she strives to become one of the insiders. If the third child were diagnosed with PANDAS, this would differentiate the third child further. As this develops, stress compounds for the child with pre-existing anxiety due to PANDAS, and then additionally as an outsider in the triangle relationship. This situation can impact children with PANDAS due to an increase of stress and anxiety. Because of its impact triangles should be taken into account to better aid affected children. Triangles, if

working properly, can also be extremely beneficial for a child with PANDAS. In a triangle relationship stress and anxiety can be reduced and changes in environment can be better managed. Sound relationships handle stress well and can reduce stress in a struggling member. The importance of this reduction of stress cannot be undermined especially in the case of a child with PANDAS, as stress and anxiety are major issues.

Differentiation of Self. In a social group like a family, there are two variables to consider in this Family Systems Theory concept: differentiation of self (the ability to separate feelings and thoughts), and the susceptibility of an individual to groupthink (irrational/dysfunctional thinking as a group) where a social group affects the way individuals in the group think and act (Kerr, 2000). When the self is less developed, the group can have more influence on that person. An inadequately differentiated self will strive for approval of their peers by tailoring actions to conform or, in the case of a bully, pressure others to conform to him or her. In the case of a properly differentiated self, a person understands that he or she might depend on others, but is level headed in situations of criticism and can adapt to environmental changes (Kerr, 2000; Brown, 1999; Bowen 1978). Kerr (2000) also delineated when there is high family member interdependence and less differentiation, a family is more vulnerable to anxiety and struggle when adapting to stress. This concept is important to consider when looking at how families impact child development. If a child receives a new and serious diagnosis, an elevated level of stress will ensue: differentiation of self can impact how the family and the child deal with the strain of the new challenge. In relation to PANDAS, if family members have decreased self-differentiation and if PANDAS arises, the family impact would be greater because of the increased susceptibility to stress. A child who develops

PANDAS is likely prepubertal and it is possible that he or she does not have a completely differentiated self. Based on family systems theory, a low differentiation of self increases vulnerability to tension and anxiety (Kerr, 2000). It is very possible that a child with PANDAS has a low differentiation of self as a child recently diagnosed is prepubertal and therefore is in Erikson's psychosocial stage of development "industry vs. inferiority" where the child strives for approval from peers and adults. A child in this stage is very similar to a child with a poorly differentiated self as in both cases there is a strive for approval. Because of this it is very plausible that a child recently diagnosed with PANDAS could have a low differentiated self as the two go hand-in-hand. These two aspects along with the disorder itself increases the vulnerability, decreases the ability to cope and potentially leads to more severe expression of symptomatology with an increase in stress and anxiety. On the other hand, if the child and family have properly and more developed differentiated selves, the group and outside situations will have less of an influence and there will be less susceptibility to anxiety. Using family to decrease anxiety can be extraordinarily therapeutic and beneficial to any child especially one suffering from an anxiety disorder.

Nuclear Family Emotional Process. This emotional process encompasses four basic patterns that reveal problems and conflicts that arise in a family. The four patterns are marital conflict, dysfunction in one spouse, impairment of one or more children, and emotional distance (Kerr, 2000). As tensions in a family rise, spouses can externalize their anxiety into relationship issues including marital conflict. Dysfunction in one spouse pressures the other into subordination, building up anxiety, and leading to medical and psychological problems. If impairment of a child develops, increased anxiety in that

child ensues due to the parents likely focusing stressful attention on the child. The parents may have had an idealized image of their child, or develop a negative view, either of which can impact the child and can be extremely harmful. Success in school, relationships, and the health of the child suffer. Emotional distance is expressed as an increased isolation in one family member, which can intensify anxiety in other members of the family. The nuclear family's emotional process is important to consider because, as Kerr (2000) notes, clinical problems can develop during times of tension and stress within the family. All four of these patterns can impact a child suddenly diagnosed with PANDAS. The child is impaired due to the disease state, leading to marital conflict as the parents try to cope with the symptoms of PANDAS. The parents would observe this "negative" change in their child, leading to potential dysfunction of one parent, and development of emotional distance as a negative coping mechanism. The child, feeling the stress of this extra negative attention might develop increased anxiety, worsening the symptoms further. However, if the parents cope well with the diagnosis, many of these additional issues can be avoided and the family can engage in a more open-minded approach to therapy, which can help the child and mitigate many of the issues associated with PANDAS. The nuclear family emotional process predominantly describes the negative impacts a family can create, but avoiding these issues can be one of the keys to helping a child meet specific challenges and overcome its obstacles. A strong marital bond helps prevent stress and other issues that can negatively impact a child.

Family Projection Process. The family projection process describes how parents project their own personal emotional problems onto a child, which increases vulnerability and clinical issues for the child (Kerr, 2000). While this analysis will look at the family

projection process predominantly in a negative light, it is important to note that the process can be both positive and negative depending on the specific situation. Kerr (2000) shows how this process occurs in three general steps: the parent fears there is something wrong with the child and turns his or her focus on the child; with confirmation bias, the parent verifies his or her fear; the parent changes his or her actions towards the child as if something is wrong with the child. These steps begin early in the child's life and can create a self-fulfilling prophecy to embody what the parent projects (Kerr, 2000). This is pertinent to PANDAS, where something about the child is imperfect, and parents likely project certain emotions onto the child, exacerbating the child's stress and symptoms. This is similar to the nuclear family emotional process. The child with PANDAS has anxiety due to the symptoms, and as parents project their own fears, that anxiety is magnified. Although this process can project issues and create a self-fulfilling prophecy, there is also an opportunity to take therapeutic advantage of the process. If the parents project positive ideas onto the child, a self-fulfilling prophecy may allow for a positive outcome in this regard. Doing this would support the child and give the child confidence to combat some of the challenges associated with PANDAS like cognitive functioning issues.

Emotional Cutoff. Emotional cutoff develops when a person has unresolved issues with another and they create an emotional separation. Cutting off creates new challenges because the person making the separation will often look at his or her other relationships to fill that void, causing other issues (Kerr, 2000). Most people have unresolved attachment issues with their caregivers, but those who are well differentiated are able to resolve those challenges (Kerr, 2000). Unresolved attachments can appear in

various forms: acting child-like when returning home as an adult, feeling guilty with parents, and showing anger that parents don't understand (Kerr, 2000). The emotional cutoff demonstrates how different aspects of child development interact. When emotional cutoff develops, a poorly differentiated child might cut off his or her caregiver due to unresolved attachment issues. If this same child has PANDAS, more complex challenges can occur. The child feels anxiety due to PANDAS, but will also be searching to fill the void created by the cutoff. Further issues may arise, and guilt will increase due to both the emotional cutoff and OCD symptoms. This two-fold guilt can have significant negative impacts on any child, especially a vulnerable, poorly differentiated, emotionally cutoff child with PANDAS.

Sibling Position. Kerr (2000) also showed how Bowen incorporated Walter Toman's (1961) theory on birth order, which discusses eleven different birth order possibilities and how each demonstrates differences in characteristics. Toman (1964) also researched birth order in relation to marriage partners and the chance of divorce based on the birth order. It is important to note that birth order research has been critically reviewed because of the lack of controls (Ernst & Angst, 1983).

Societal Emotional Process. This piece of Bowen's Family Systems theory shows that the other seven concepts can be used in non-family groups in society. This concept is less pertinent to the content of this review, but it is still important to note this piece of the theory.

The Benefits to the Family in Family Systems Theory. Each concept has its advantages and disadvantages in a family. A caring family that recognizes an issue and seeks further assistance will aid a child with PANDAS tremendously. Seeking help and

learning about ways the family impacts the child who develops PANDAS will benefit the child by decreasing issues that can arise in the family. Alternatively, if a family accommodates, the family contributes to maintaining a disorder like OCD by allowing symptoms and rituals to continue and even worsen (Calvocoressi et al., 1995).

4) With an understanding of family systems theory, how does the family affect OCD treatment? What lessons can be learned for PANDAS?

Family Accommodation in Pediatric OCD. Family accommodation of symptoms is defined as parents and families accommodating, allowing, and facilitating the continuation of symptoms and rituals that their children present (Calvocoressi et al., 1995). Currently, there is little if any research concerning family accommodation in PANDAS children. However, there is extensive research in Obsessive-Compulsive Disorder (OCD) and family accommodation (Calvocoressi et al., 1995; Lebowitz & Bloch, 2012; Wu, McGuire, Martino, Phares, Selles, & Storch, 2016a; McGuire et al., 2015; Allsopp & Verduyn, 1990). The literature on family accommodation and the role of the family in children with OCD elucidates how certain aspects might be similar to or different from families with a child diagnosed with PANDAS.

Pediatric OCD is understood as recurrent thoughts and/or repetitive behaviors that result in distress and impaired functioning (American Psychiatric Association, 2000). Family accommodation in OCD can be seen in different forms and is characterized by modifying family routines, facilitating avoidance of OCD triggers, and even engaging in the child's compulsions (Calvocoressi et al., 1995). An example of engaging in compulsions is when a parent washes their hands with their child a dozen times, hoping to reduce their child's stress and guilt in the compulsive situation. Family

accommodation might be promising to not throw certain items away, abiding by specific timetables, and allowing touch rituals (Lebowitz & Bloch, 2012). When these accommodations occur, a cycle begins and the parents unintentionally perpetuate the symptoms, preventing the child from using alternative coping mechanisms (Wu et al., 2016a). Unfortunately, family accommodation goes directly against the main goal of treatment for OCD (American Academy of Child and Adolescent Psychiatry, 2012; McGuire et al., 2015). One study found that seventy percent of parents report that they are involved in their child's symptoms (Allsopp & Verduyn, 1990).

Due to the nature of OCD and how the family is involved in its symptoms, family life is impacted (Black, Gaffney, Schlosser, & Gabel, 1998; Valderhaug & Ivarsson, 2005). The family is so involved in a child's OCD compulsions that there is evidence that links the accommodation to negative family outcomes, poorer general functioning, lack of organization and harmony, as well as increased burden on the family (Amir, Freshman, & Foa, 2000; Steketee & Van Noppen, 2003; Ferrao et al., 2006; Futh, Simonds, & Micali, 2012; Albert et al., 2010; Maina, Saracco, & Albert, 2006; Peris et al., 2008; Steketee, 1997; Erol, Yaziel, & Toprak, 2007). It is important to consider the impact on both the child and the family.

Storch et al. (2007a) conducted an extensive study examining family accommodation and pediatric OCD. The sample included 57 children diagnosed with OCD with a mean age of 12.99 ± 2.54 and included 50 mothers and 7 fathers. The study used several measures to examine the severity of family accommodation (Wu et al., 2016b), assess obsession severity (Scahill et al., 1997; Storch et al., 2004), study the extent to which OCD symptoms impact the child the most (Piacentini, Bergman, Jacobs,

McCracken, & Kretchman, 2002; Piacentini, Bergman, Keller, & McCracken, 2003), and measure the internalizing and externalizing symptoms (Achenbach, 1991). Storch et al., (2007a) found family accommodation was not related to child age or gender, but was correlated with symptom severity and behavior ratings. The Family Accommodation Scale total score was significantly associated with Children's Yale-Brown Obsessive Compulsive Scale and the Child Behavior Checklist scores, meaning family accommodation was associated with the child's OCD symptom severity. The researchers found an association between family accommodation and parent-ratings of the child's functional impairment, but no relationship with the child-reported functional impairment. Child functional impairment was correlated with parent ratings, but not child ratings. The children did not think that they were impaired, which is interesting because most studies, including this one, find increased functional impairments in family accommodation. This means that it has been determined that children with OCD are impaired, but at the time the children do not view themselves as impaired.

Further proof that family accommodation is related to increased OCD symptom severity was confirmed through a meta-analysis performed by Wu et al. (2016a). This connection is interesting because, although well intentioned, the accommodation of symptoms increases severity of OCD symptoms in children.

When evaluating treatment options, it is important to consider the correlation of accommodation and the ability of the child with OCD to benefit from treatment.

Cognitive behavioral treatments and psychopharmacology have been seen as successful treatment options for children with OCD (King, Leonard, & March, 1998). Despite this success, there are a significant number of children who do not improve with these

treatments. Family accommodation can impede treatment, as demonstrated by the Pediatric OCD Treatment Study Team (OCDTST; 2004) and Garcia et al. (2010) who found that increased family accommodation lead to poorer treatment outcomes. This limit on treatment success shows that families, especially parents, should be included in treatment therapy. With proper treatment it has been shown that family accommodation can be reduced (Storch, Lehmkuhl, Ricketts, Geffken, Marien & Murphy, 2010; Storch et al., 2007a; Barrett, Healy-Farrell, & March, 2004; Waters, Barrett, & March, 2001). Family plays a vital role in the life of a child with OCD and in the disorder as a whole.

Although this focused on the negative impact of family accommodation, it is important to see the impressive positive impact a family can have on a child with OCD. For example, when compulsions like hand-washing begin to take over, a family can accommodate by distracting the child from triggers. This can be done through physical activity, like a parent playing basketball with the child or even going for a walk. In this way the family accommodation is helpful and reduces compulsions by reducing triggers and occupying time.

Discussion of How Family Accommodation in OCD Relates to PANDAS.

There is extensive information and research about the family impact on a child diagnosed with OCD and its relationship to family accommodation. I have attempted to address the following question: How does the family impact on a child with PANDAS compare to the impact of a child with OCD? Based on the information presented on the family impact on a child with OCD, I will speculate on the impact in PANDAS.

Because the primary symptom of PANDAS is OCD, there are often misdiagnoses, and some clinicians may not use the PANDAS diagnosis at all. One of the most

significant differences between these diagnoses is the timing of symptoms at onset. OCD has a gradual onset whereas PANDAS is acute. PANDAS develops so suddenly that many call it “overnight” where parents know the exact day symptoms arose (Jenike & Dailey, 2014). The sudden onset leaves the parents and families unprepared for their child’s disorder.

This profound difference in rapidity of onset can lead to increased family impact through family accommodation and exacerbated reaction. As in the case of OCD, there is often family accommodation that facilitates, maintains, and increases the severity of the disorder. The quick onset of PANDAS may increase the distress of the family. Parents might be more inclined to accommodate their child with their compulsions with hopes of decreasing the short-term distress. While cases of OCD allow parents some adjustment time due to the gradual onset of symptoms, parents will be less prepared with PANDAS and may accommodate to an even greater degree.

If parents feel more motivated to accommodate their child, the rituals and compulsions will continue as they are maintained by the family. Based on presented trends, this will impact functional impairment, family life, severity of symptoms and more. The similarities between the two disorders and the implications of family accommodation intensify family issues in children with PANDAS. I believe that the family impact of PANDAS will be similar to but more severe than that of OCD.

Discussion of Framing and Reframing with PANDAS and OCD. In consideration of the similarities and differences when framing and reframing in PANDAS and OCD, parental attitudes may come into play. PANDAS can be thought of as a biological disorder, while OCD is a psychiatric disorder. In this, parents could

perceive PANDAS as something they cannot do anything about because it is biological and therefore cannot be changed. Because OCD is perceived to be a psychiatric condition, parents might think this can be treated through psychotherapy. With this, framing and reframing can be important. If PANDAS can be reframed from a biological to a psychiatric disorder, parents will be more likely to pursue therapy and treatment options. Reframing how PANDAS is perceived can have an impact on the mitigation of symptoms in a child with PANDAS because it can allow for parents to more readily pursue beneficial treatment options. This is speculation, but it sheds light on important considerations in family systems theory through framing and reframing.

Conclusion and Areas of Future Research

Since first described by Swedo et al. in 1998, research in PANDAS has increased dramatically. Many aspects of the disorder have been carefully examined, but there are still many unanswered questions concerning the etiology and treatment of PANDAS. The most basic yet challenging question is whether PANDAS is a condition independent of other diagnoses like childhood OCD.

There are two topics critical to the advancement of the field of PANDAS. The first is to differentiate PANDAS from other disorders like OCD. With several options, the two primary aspects for future research examine the possible causal relationship between Streptococcal infections and the onset of PANDAS, and search for definitive biomarkers establishing PANDAS as a unique disorder. As presented in this paper, many studies have attempted to look into these two facets. These studies have been inconclusive and more work is needed. A large systematic study of children recently

diagnosed with PANDAS would have the potential to better establish the relationship between prior Streptococcal infection and onset of symptoms.

In the nearer future, researchers could more easily evaluate family impact and family accommodation in PANDAS. Comprehensive research on this topic in OCD has been conducted and many tools have been created to study family accommodation, like the Family Accommodation Scale, the Children's Yale-Brown Obsessive Compulsive Scale, the Child Obsessive Compulsive Impact Scale, and the Child Behavior Checklist. These scales assess family accommodation as they relate to severity of symptom like compulsions and rituals. Because these scales already exist they can be utilized on a population of children diagnosed with PANDAS and their families. With the use of these tools, PANDAS family accommodation would be evaluated directly rather than inferred using data on OCD family accommodation. If studied in combination with family systems theory, treatment options might be significantly improved as family factors could be used more specifically for PANDAS-affected families. In understanding family accommodation through a family systems theory lens, the various impacts a family has on a child with PANDAS can be examined to improve therapies, understand more, and most importantly help the children and families impacted by the disorder.

There is significant opportunity for important research in the rapidly expanding field of PANDAS. As more is learned about the pathogenesis, biomarkers, family impact, family accommodation and all of the disorder's intricacies, the field can help children and families impacted by this challenging disorder.

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