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Disordered Eating and Food Restrictions in Children with PANDAS/PANS

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Abstract

Objective: Sudden onset clinically significant eating restrictions are a defining feature of the clinical presentation of some of the cases of pediatric acute-onset neuropsychiatric syndrome (PANS). Restrictions in food intake are typically fueled by contamination fears; fears of choking, vomiting, or swallowing; and/or sensory issues, such as texture, taste, or olfactory concerns. However, body image distortions may also be present. We investigate the clinical presentation of PANS disordered eating and compare it with that of other eating disorders.

Methods: We describe 29 patients who met diagnostic criteria for PANS. Most also exhibited evidence that the symptoms might be sequelae of infections with Group A streptococcal bacteria (the pediatric autoimmune neuropsychiatric disorder associated with streptococcal infections [PANDAS] subgroup of PANS).

Results: The clinical presentations are remarkable for a male predominance (2:1 M:F), young age of the affected children (mean = 9 years; range 5–12 years), acuity of symptom onset, and comorbid neuropsychiatric symptoms.

Conclusions: The food refusal associated with PANS is compared with symptoms listed for the new *Diagnostic and Statistical Manual of Mental Disorders,* 5th ed. (DSM-V) diagnosis of avoidant/restrictive food intake disorder (ARFID). Treatment implications are discussed, as well as directions for further research.

Introduction

In addition to the sudden overnight onset of classic obsessive-compulsive symptoms, the sudden onset of reduced and restricted food intake is one of the defining diagnostic symptoms of pediatric acute-onset neuropsychiatric syndrome (PANS) (Swedo et al. 2012). Multiple etiologies for PANS have been hypothesized, ranging from genetic and immunologic disorders to postinfectious sequelae. When the symptoms are preceded by a group A streptococcal (GAS) infection, the condition is referred to as ''pediatric autoimmune neuropsychiatric disorder associated with streptococcal infections'' (PANDAS) (Swedo et al. 1998). In 1997, Sokol and Gray described the first cases of ''PANDAS anorexia'' (PANDAS-AN) in their eating disorders unit at the Menninger clinic (Sokol and Gray 1997). Notably, the PANDAS-AN patients described were prepubescent, feared weight gain as a result of body dysmorphic issues, and exhibited symptoms temporally related to a GAS infection. Additional reports document positive GAS cultures among youth with abrupt onset of choking fears and refusal to swallow (Henry et al. 1999). These observations contribute to a growing body of literature documenting that viral and bacterial infections can precipitate acute-onset food restriction (Patton et al. 1986; Park et al. 1995; Sokol and Gray 1997; Simon 1998; Sokol 2000, Watkins et al. 2001; Storch et al. 2004; Calkin and Carandang 2007). Systemic diseases, including autoimmune disorders such as systemic lupus erythematosus (Toulany et al. 2014), have also been reported to cause food restrictions via immune dysregulation. Anorexia nervosa (AN) has also been postulated to result when disease-related loss of appetite produces excessive weight loss (Dally 1969; Beumont et al. 1978) and subsequent development of body image distortions.

In youth with PANDAS, food restriction has been reported to occur in the context of obsessional fears about contamination, as well as in the context of the sudden onset of fears of swallowing, choking, or vomiting that are often associated with sensory phenomena (e.g., the perceived texture or appearance of the food). In rare instances, these fears lead to the child's refusal to ingest anything orally including any liquids. Contamination fears may lead to dietary restriction of all or selected food items (Bernstein et al. 2010). For example, a child with PANDAS was reported to

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have a fear of choking and contamination that led to complete cessation of food consumption and loss of 10% of the subject's body weight (Storch et al. 2004). Another report detailed the abrupt onset of obsessions about choking, accompanied by refusal to swallow, in association with a positive GAS culture (Henry et al. 1999). Restricted eating also has been reported to occur secondary to new onset of body image distortions of being ''too fat'' or not having a ''six-pack'' (Swedo et al. 2012). To date, little has been published on food restrictions in PANS. We report experience with 29 patients who met criteria for PANS and who also exhibited acute-onset food restriction.

Methods

The patients described in this series were participants in clinical trials at the National Institute of Mental Health (NIMH) or at the Rothman Center of Neuropsychiatry at the University of South Florida (USF). All subjects met criteria for PANDAS or PANS and reported new, abrupt onset of eating restrictions or food avoidance. Children participating in the NIMH trial ($n=16$) were among a larger cohort enrolled in a study of intravenous immunoglobulin (IVIG) for the treatment of PANDAS (NCT01281969). This study was approved by the National Institutes of Health (NIH) Central Nervous System (CNS) institutional review board (IRB); parents provided informed consent and children provided assent for study participation. Children included from USF ($n=13$) were from three studies, with most from a larger cohort of participants in a study investigating azithromycin as a PANS treatment ($n=10$; NCT01617083, 6119-128500). These studies were approved by the USF-affiliated IRB; parents provided informed consent and children provided assent for study participation. All of the patients met full criteria for PANS; some also had evidence of preceding GAS infections and, therefore, met criteria for PANDAS. Pertinent subject data are summarized in Table 1.

Assessments

Symptom severity was measured using the Children's Yale-Brown Obsessive Compulsive Scale (CY-BOCS) (Scahill et al. 1997) and Yale Global Tic Severity Scale (YGTSS) (Leckman et al. 1989). All assessments were conducted or reviewed by trained clinicians with experience in pediatric obsessive-compulsive disorder (OCD) and tic disorders. Comorbidity symptoms were collected at both sites using PANS/PANDAS checklists as well as symptoms deemed present in the clinical evaluation.

Laboratory tests for streptococcal infection included anti-DNase B and antistreptolysin O (ASO) titers. Because of differences in laboratory standardization, thresholds of elevation differed between sites. Thresholds used to designate groups into elevated or unelevated categories at each site were as follows: ASO > 160 IU/mL for ages 0–6 and > 200 IU/mL for ages 7–17 (USF); ages 5–17 years > 640 IU/mL (NIMH); anti-DNase B > 60 U/mL for ages 0–6 and > 170 U/mL for ages 7–17 (USF); > 375 U/mL (NIMH). Assays were performed by the USF clinical research laboratory, or for NIMH subjects, Mayo Medical Laboratories in Rochester, Minnesota.

Results

Twenty-nine children are the subjects of this report, including 20 males (69%) and nine females (31%), with mean age of 9 years (range 5–12 years). All children reported obsessive-compulsive symptoms, with an average CY-BOCS = 30.1 (± 5.2 SD). Eighteen children had tics, with an average YGTSS = 16.6 (± 7.9 SD) (see Table 1). Two thirds ($n=19$) of the children (66%) reported that their food restrictions were secondary to contamination fears (see Table 2). Of those with contamination fears, 12 had fears involving germs, three had fears involving poison, and one each had fears of allergens, bleach, illicit drugs, or ''the essence and personality of other people.'' Others expressed fears of vomiting (28%, $n=8$) or choking (21%, $n=6$). In addition to food restriction, five patients (17.2%) refused to swallow their own saliva, and another five refused all food for several days or longer. Three children (10%) expressed concerns about weight or body shape. Mean change in weight (in pounds) was - 4.21 (± 5.85 SD) and mean percent body weight change was - 4.89% (1.91 kg ± − 2.66 SD). In the USF sample, 12 out of 13 cases, and in the NIMH sample 14 out of 16 cases, had generalized OCD in addition to food restriction. Mean illness duration was 2.68 months (± 1.68 SD). For PANS neuropsychiatric symptoms, see Table 3.

Eighteen children (62%) were confirmed to have had a positive rapid GAS test or culture at or near the time of PANS onset (See Table 1). Six youth had been exposed to GAS. Mycoplasma pneumonia (MP) exposure or infection was evident in 4 of 12 children examined, 3 of whom (all male) had positive MP immunoglobulin (Ig) G and negative MP IgM, and 1 of whom (female) had positive MP IgG and IgM. A few children had more than one reported infectious trigger.

Selected cases

Patient 8. Patient 8 was an 8-year-old male who presented to USF 1 month following the sudden onset of severe acute-onset contamination fears, food refusal, and tics. Past medical history was significant for a viral infection (gastrointestinal [GI] symptoms) immediately preceding the PANS symptoms, and a lifetime history of frequent GAS infections leading to adenotonsillectomy. Premorbid psychiatric history was notable for attention-deficit/ hyperactivity disorder (ADHD) and minor separation anxiety disorder (SAD). Physical examination was only remarkable for moderate livedo reticularis. The patient started having fears of dying suddenly while he and his family were at a restaurant. He thought he was having an allergic reaction, and despite efforts to assuage his anxiety, he began having a panic attack. Although he had no history of food allergies, he then developed contamination fears related to allergens in food, and he refused to eat most solid food. His mother reported that when she attempted to give him dry toast, he refused to eat it and began to dry heave. In addition to allergens, he expressed concern that ''other people's medications'' were in his food. At evaluation 1 month post-onset, the parents reported that the child had lost 2 lb (3% of his body weight). All laboratory values were within normal limits, including streptococcal and mycoplasma titers. Out of a desperate desire to get him to eat, his mother began giving him fake allergy pills (i.e., Sweet Tarts), so that he would eat more. However, this measure soon failed, and the boy's contamination fears generalized to the point where his intake was limited to clear liquids. He was started on azithryomycin treatment and, within 1 month, his worries about allergens and medication poisoning were near remission, and he was eating and drinking normally.

Patient 12. Patient 12 was a 10-year-old male with a past history of ADHD, who presented at NIH with sudden-onset severe OCD and a specific fear that his hands and lips were contaminated with bleach cleaner. He had tested positive for GAS and had been

Table 1. Patient Demographics, Premorbid History, Baseline Scores, and Laboratory Results

Patient	*Sex*	*Age at evaluation*	*Premorbid psychiatric history*	*Medical history*	*History of infection or exposure*	*CYBOCS*	*YGTSS*	*ASO*	*Anti-DNase B*
1	F	5	-	Croup T&A	Exposure to viral meningitis	37	26	NL	NL
2	F	8	SAD (mild) skin picking age 2)	-	Confirmed mycoplasma pneumonia	30	0	NL	NL
3	M	9	Tics (mild)	Frequent GAS and URIs Eczema	Confirmed GAS	29	16	NL	↑
4	M	5	-	Frequent staphylococcal infections	Exposure to GAS	35	9	↑	↑
5	M	8	-	Frequent GAS Frequent URIs	Confirmed GAS	31	0	NL	↑
6	M	11	-	Frequent GAS	Confirmed GAS	13	0	↑	↑
7	M	12	Tics (mild)	Asthma Frequent GAS	Exposure to GAS	33	16	↑	↑
8	M	9	ADHD SAD (mild)	Frequent GAS T&A	Exposure to virus	31	9	NL	NL
9	M	9	-	Frequent GAS	Confirmed GAS	34	0	↑	↑
10	F	12	-	Frequent URIs	Confirmed mycoplasma pneumonia	37	0	↑	NL
11	M	12	Tics (mild)	Asthma Allergies	Chronic URIs	29	34	NL	NL
12	M	10	ADHD	Allergies	Confirmed GAS	31	9	NL	NL
13	F	8	-	-	Exposure to GAS (rapid antigen detection negative)	27	18	↑	↑
14	M	7	ADHD Sensory integration disorder Speech delay Tics (mild)	Infantile febrile seizures Eczema	Confirmed GAS	27	4	NL	NL
15	M	12	-	Asthma Frequent GAS	Confirmed GAS	24	0	NL	NL
16	M	11	Speech delay	Asthma	Confirmed GAS	28	15	↑	↑
17	M	10	-	Frequent GAS Frequent otitis media PE tubes	Confirmed GAS	28	12	↑	↑
18	M	7	-	Frequent GAS Frequent otitis media PE tubes	Confirmed GAS	25	0	NL	↑
19	F	9	Anxiety	Asthma Borderline adrenal suppression (secondary to inhaled corticosteroids) Borderline hypothyroidism Frequent GAS	Confirmed GAS	32	0	NL	NL
20	M	8	-	Frequent otitis media Scarlet fever	Confirmed GAS	37	0	↑	NL
21	F	6	-	-	Exposure to GAS (rapid antigen detection negative)	31	13	↑	↑
22	F	7	-	GERD	Exposure to GAS (rapid antigen detection negative)	34	18	NL	NL
23	M	12	-	-	Confirmed GAS	36	29	↑	↑
24	F	8	-	Asthma Food allergies	Exposure to GAS (rapid antigen detection negative)	31	21	NL	NL

(*continued*)

Table 1. (Continued)

Patient	*Sex*	*Age at evaluation*	*Premorbid psychiatric history*	*Medical history*	*History of infection or exposure*	*CYBOCS*	*YGTSS*	*ASO*	*Anti-DNase B*
25	M	12	-	Frequent GAS Tonsillectomy	Confirmed GAS	22	0	NL	NL
26	F	9	-	-	Confirmed GAS	27	19	NL	NL
27	M	10	ADHD	PE tubes T&A	Confirmed GAS Confirmed Influenza	33	8	N/A	N/A
28	M	6	-	Frequent GAS Frequent otitis media T&A Tics with EBV	Confirmed GAS	35	23	↑	↑
29	M	9	-	Frequent GAS Frequent otitis media	Confirmed GAS	26	0	↑	NL

CYBOCS, Children's Yale-Brown Obsessive Compulsive Scale; YGTSS, Yale Global Tic Severity Scale; ASO, antistreptolysin O; SAD, separation anxiety disorder; T&A, tonsil and adenoid surgery; GAD, generalized anxiety disorder; URI, upper respiratory infection; ADHD, attention-deficit/hyperactivity disorder; PE, pressure equalizer, GERD, gastroesophageal reflux disease; EBV, Epstein–Barr virus.

exposed to siblings who tested positive for GAS prior to his sudden onset of symptoms. The GAS infection was treated with a 5 day course of azithromycin. After the children's GAS infections, their mother cleaned the house with bleach, and shortly afterwards, the patient developed an obsession that any food he touched would become contaminated with bleach, harming or killing him. Even when his mother removed all bleach from the house, the child no longer allowed her to prepare his food, as he believed she was ''contaminated.'' When his father performed yard work using fertilizer, the child believed that his father was also now ''contaminated.'' The child began to spit out or throw away any food that touched his hands or lips. He constantly sought reassurance from his parents by asking, ''Is this bleach? Will bleach kill me?'' In addition, he engaged in excessive showering, hand washing, and tooth brushing behaviors. He would only eat food that was cut into long ''french fry'' shapes so that he could pass the food into his mouth without it touching his lips, and eventually he refused to eat completely. This contamination fear generalized to the point that he would not swallow even his own saliva, and would instead hold his saliva in his mouth at school until he could go to the bathroom and spit it out. Because of intense contamination fears, the child had restricted his caloric intake to between 800 and 1000 calories daily, without expressed desire to lose weight or dissatisfaction with his body. He also reported feeling hungry and was distressed by his inability to eat, even expressing suicidal ideation when frustrated.

Upon entering the NIH study, this child was prescribed penicillin as prophylaxis against future GAS infections, and 2 g/kg of IVIG over a course of 2 days. Six weeks later, the patient and his parents reported a 90–95% improvement in his symptoms.

Patient 13. Patient 13 was an 8-year-old female who had a sudden onset of OCD symptoms including excessive confessing, concern with right and wrong, and contamination fears. She had been exposed to GAS at school, and she and her fraternal triplet sisters had flu-like symptoms, but she cultured negative for GAS pharyngitis. At her baseline visit at NIH, her ASO was 403 (normal for age), and anti-DNAse B was elevated at 397. Historically the ''healthiest'' of her siblings, the patient experienced a drastic change in personality, with extreme perfectionism and concern with morals. She constantly confessed to doing something ''wrong'' or ''bad'' on purpose, when in fact she had done nothing. She constantly apologized and expressed guilt about supposed transgressions and would hit herself on the head or engage in other self-injurious behaviors.

At the time of presentation to NIH, the child's overscrupulosity had escalated to the point that she felt she ''did not deserve to eat'' or do other pleasurable things such as watch television. She especially refused to eat foods that she considered ''treats,'' such as cookies and other foods with sugar. She insisted that her mother not pack treats in her lunch, and if her mother packed a treat anyway, the child refused to eat it and would bring it home or give it away to friends. During the structured interview, she admitted that she was somewhat preoccupied with her appearance and thought that an unrealistically thin doll represented an ideal to which to aspire.

This patient was prescribed a 2 week course of amoxicillin by an outside physician ~ 3 weeks after symptom onset. Two weeks later (and 4 weeks prior to study enrollment), amoxicillin-clavulanic acid was started by an outside physician for GAS prophylaxis; this medication was continued throughout the duration of NIH study participation as well. At NIH, this patient was treated with IVIG per protocol at baseline and 6 weeks, and made a full recovery with only slight residual generalized anxiety. Her parents reported that she was still a selective eater, but that her food intake was adequate.

Patient 24. Patient 24 was a 7-year-old girl with unremarkable premorbid medical or psychiatric history who presented to NIH with complaints of acute-onset OCD that began 9 months prior to evaluation. At that time, she abruptly displayed a compulsive need to carry a plastic bucket at all times secondary to fears of vomiting. She expressed fears of choking, and subsequently refused to eat for 3 consecutive days. She developed fear of contaminants and fear that harm might come to her. She also became uncharacteristically irritable and aggressive, and she displayed severe separation anxiety, behavioral regression, inattentiveness, hyperactivity, and insomnia. A rapid GAS test performed at that time was negative, but she was prescribed cephalexin. The cephalexin had no discernible therapeutic effect; therefore, 5 days later the child's pediatrician discontinued cephalexin and prescribed a course of amoxicillin. Within 36 hours of starting amoxicillin, the child was described as ''90% back to normal'' according to her parents. Amoxicillin was continued for 6 weeks, then stopped for 5 days, but was resumed because of worsening behavior and anxiety, and then

Table 2. Food-Related Symptoms and Behaviors

Patient	*Sex*	*Age at evaluation*	*Food-related fears*	*Food-related behaviors*	*ΔWeight in kilograms (% body weight change)*	*Illness duration*
1	F	5	Contamination fears: Germs; fear of vomiting	Restrictive eating	0	3 months
2	F	8	Fear of choking	Refusal of solid food; refusal to swallow saliva	−2.3 (10)	3 months
3	M	9	Contamination fears: Germs; fear of vomiting	Refusal to eat unless father is present	+2.3 (4)	2 months
4	M	5	Fear of choking or vomiting	Restrictive eating	−1.8 (9)	4 months
5	M	8	Contamination fears: Poison	Restrictive eating	0	1 month
6	M	11	Disgusted by smell and taste of food	Restrictive eating	−1.4 (4.6)	2 months
7	M	12	Contamination fears: Illicit drugs	Restrictive eating	−7.7 (14)	3 months
8	M	9	Contamination fears: Allergens	Restrictive eating	−0.9 (3)	6 months
9[a]	M	9	Contamination fears: Germs	Refusal to consume food that has been in his home	−1.8 (6)	1 month
10[a]	F	12	Contamination fears: Germs	Refused to eat or drink for 3 days; refusal to eat or drink unless preparing it herself	−5.9 (11)	2 months
11	M	12	Contamination fears: ''Essence'' of others in food	Restrictive eating; refusal to swallow saliva	−3.6 (8.3)	2 months
12	M	10	Contamination fears: Bleach	Would not allow food to touch his lips; eventual refusal of solid food; refusal to swallow saliva	Yes (value unavailable)	1 month
13	F	8	Feeling she didn't deserve to eat or do pleasurable things, body image concerns	Restrictive eating	Yes (value unavailable)	2 months
14	M	7	Contamination fears: Poison	Restrictive eating; refusal to swallow saliva	Yes (value unavailable)	2.5 months
15	M	12	Contamination fears: Germs	Restrictive eating	0	5 months
16	M	11	Contamination fears: Poison	Refusal to eat for days	0	5 months
17	M	10	Contamination fears: Germs	Restrictive eating	0	8 months
18	M	7	One episode of fear of choking	Decrease in appetite	0	3 months
19	F	9	Contamination fears: Germs	Restrictive eating and drinking	−1.8 (4.5)	<1 month
20	M	8	Contamination fears: Germs; fear of vomiting	Restrictive eating	0	3 months
21	F	6	Fear of choking	Restrictive eating	Yes (value unavailable)	3 months
22	F	7	Would not disclose; concerns about being overweight	Restrictive eating	Yes (value unavailable)	1 month
23	M	12	Contamination fears: Germs; fear of vomiting	Restrictive eating	−1.8 (4)	4 months
24	F	8	Contamination fears: Germs; fear of vomiting; fear of choking	Refusal to eat for 3 days	0	1.5 months
25[a]	M	12	Fear of vomiting	Refusal to eat for days	−5.9 (13)	2 months
26	F	9	Fear of vomiting	Restrictive eating	0	1 month
27	M	10	Fear of choking; Concerns of being overweight	Refusal to eat; refusal to swallow saliva	−7.7 (18)	3 months
28	M	6	Contamination: Germs	Restrictive eating; ritualized eating patterns	−4.5 (13)	1 month
29	M	9	Contamination: Germs; Concerns of being overweight	Restrictive eating	−0.9 (3)	2 months

[a]Indicates child was hospitalized secondary to dehydration.

Table 3. Acute-Onset Neuropsychiatric Symptoms

	Total (%) (n = *29*)	*M (%)* (n = *20*)	*F (%)* (n = *9*)	*NIMH (%)* (n = *16*)	*USF (%)* (n = *13*)
Mood lability	26 (90%)	18 (90%)	8 (89%)	15 (94%)	11 (85%)
Inattention and/or hyperactivity	23 (80%)	14 (70%)	9 (100%)	14 (88%)	9 (69%)
Separation anxiety	22 (76%)	14 (70%)	8 (89%)	15 (93%)	7 (54%)
Behavioral regression	20 (69%)	15 (75%)	5 (56%)	12 (75%)	8 (62%)
Tics	19 (66%)	12 (60%)	7 (78%)	11 (69%)	8 (62%)
Dysgraphia	15 (52%)	9 (45%)	6 (67%)	8 (50%)	7 (54%)
Oppositional or aggressive behaviors	14 (48%)	8 (40%)	6 (67%)	10 (63%)	4 (31%)
Enuresis/Frequent urination	13 (45%)	9 (45%)	4 (44%)	7 (44%)	6 (46%)
Sensory sensitivity	12 (41%)	7 (35%)	5 (56%)	6 (38%)	6 (46%)
Psychosis	6 (21%)	5 (25%)	1 (11%)	3 (19%)	3 (23%)

M, male; F, female; NIMH, National Institute of Mental Health; USF, University of South Florida.

continued for the next 5 months. Following exposure to a relative with a documented GAS infection, her symptoms suddenly returned and again included restricted eating secondary to contamination fears and obsessions about choking. Rapid GAS testing was negative, and a culture was not obtained. Amoxicillin was continued during this time, and a brief course of azithromycin was added by the child's pediatrician. Amoxicillin was continued during NIH study enrollment, and in conjunction with a blinded infusion of sham IVIG/placebo, produced a similar reduction in symptom severity over the course of 8 weeks.

Discussion

The children in this case series displayed acute-onset food restriction, and concomitant obsessions about contamination, poisoning, vomiting, or choking. In some instances, disordered eating appeared secondary to sensory issues or body image distortions. In addition to restricted food intake, the children also reported compulsive ways of preparing food (e.g., cutting, smelling, arranging, and ''decontaminating'' food), restricting (e.g., avoiding foods bases on texture, color, smell), or refusing food. Two thirds of the children had obsessive fears about contaminated food or beverages, and five refused to swallow their saliva because of contamination concerns.

Eighteen of the 29 cases (62%) had documented GAS infections at or shortly prior to the onset of behavioral symptoms; the remaining 11 children had evidence of GAS exposure ($n = 6$) or had another infection ($n = 5$). Evidence of recent exposure to MP was demonstrated in one patient with a positive MP IgM (MP has been implicated in the development of neurologic sequelae [Yiş et al. 2008]). Notably, MP has been considered in the pathogenesis of tic disorders (Müller et al. 2000, 2004) and is a proposed trigger for PANS (Swedo et al. 2012). Secondary symptoms such as enuresis, sleep disturbance, anxiety, and mood lability, as well as adventitious movements, are commonly associated with the onset of PANS (Bernstein et al. 2010) and were frequently present in these cases (see Table 3).

Molecular mimicry is one theory proposed in the etiology of PANDAS (Kirvan et al. 2006) and also has been postulated as a mediating factor in the development of restrictive eating disorders (Fetissov et al. 2005), as it is hypothesized that antibodies will cross the blood–brain barrier and provoke new onset psychiatric and neurological symptoms. Research has suggested that eating disorders may be associated with autoantibodies against α-melanocyte stimulating hormone, which is involved in appetite regulation, body weight, motivated behavior, and mood (Fetissov et al. 2005). Furthermore, animal models of antibodies to α-melanocyte stimulating hormones have been found to correlate with feeding behavior (Coquerel et al. 2012). OCD and anorexia are highly comorbid disorders, and structural and metabolic changes in the putamen and caudate have been found in both groups (Rubenstein et al. 1992; Harrison et al. 2009; Radua et al. 2010; Kaye et al. 2011; Rothemund et al. 2011; Friederich et al. 2012). In addition, antiputamen antibodies have been discovered in children with OCD behaviors (Kirvan et al. 2006) and in adolescents with anorexia; serum positivity was found in 6 out of 22 subjects with AN, five of whom had comorbid OCD (Harel et al. 2001), suggesting there may be a role of autoantibodies and immune factors in AN.

Avoidant and restrictive food intake disorder (ARFID) is a new diagnosis in *Diagnostic and Statistical Manual of Mental Disorders, 5th ed.* (DSM-V) (American Psychiatric Association 2013). Like other DSM-V disorders, the diagnostic criteria for ARFID describe a specific clinical presentation, without regard for etiology, response to treatment, comorbid symptoms, or even acuity of onset. The PANS cases described in this series met ARFID criteria, as there was a clear eating or feeding disturbance that led to inadequate food intake, accompanied by weight loss in some patients, and significant psychosocial dysfunction in all patients. Nearly all of the children in our series had a paralyzing fear of some adverse consequence of eating normally, as many felt food was poisoned or contaminated, or they had a fear they would vomit or choke. Only three children expressed concerns about body image or ''getting fat,'' but these obsessions developed later in the course of their symptoms. Because the children were so young, weight loss that would be trivial in an adult (e.g., 1–3 kg) may have been physiologically significant, and the children were at higher risk of dehydration and electrolyte disturbances. One child was hospitalized secondary to dramatic weight loss, and another required intravenous hydration.

As is shown in Table 4, ARFID would seem to capture the eating disturbances described previously more accurately than AN or another specified feeding or eating disorder. ARFID can be diagnosed with other psychiatric diagnoses such as OCD or pseudodysphagia if the food restriction or avoidance is severe enough to be of clinical focus, or is an extreme characteristic of the comorbid disorder. In addition, psychiatric conditions, including food restriction secondary to reactive attachment disorder, autism spectrum disorder, trauma associated with choking, and specific phobia must be considered, as symptoms of ARFID can be attributed to these primary diagnoses alone (Kreipe and

Table 4. Comparison of AN, PANDAS "Anorexia," ARFID, and PANS Disordered Eating

	AN	*PANDAS "anorexia"*	*ARFID*	*PANS disordered eating*
Onset	Insidious and usually pubertal or postpubertal[a,b]	Acute and prepubertal[c,d,e]	Acute and prepubertal (most common)[f,g,h]	Acute and prepubertal
Prevalence	Females > > Males[i]	Females > Males[c,d,j]	Females = Males[k]	Females < Males
Trigger	Genetic predisposition, neurochemical imbalance, cultural pressure[a,l]	Infection, genetic predisposition[c,d,e]	Environmental, temperamental, genetic and physiological[f,g,h]	Infection
Fears	Fears of being "fat," fear of weight gain; body image distortions[a]	Contamination, sensory, irrational thinking (e.g., food seems inedible, mechanical swallowing, food smells)[e]	Sensory, lack of interest in food; conditioned negative response to food[f,g,h]	Contamination, sensory, irrational thinking (e.g., food seems inedible, mechanical swallowing, food smells)
Resolution of symptoms and weight restoration	Slow, relapse common, high mortality rate[m]	Relatively rapid with PANDAS symptoms[c,d,e]	Slow, need to address co-morbidities [f,g,h]	Relatively rapid with PANS symptoms

[a]Kaye 2008; [b]Klein and Walsh 2003; [c]Sokol 2000; [d]Sokol and Gray 1997; [e]Calkin and Carandang 2007; [f]Fisher et al. 2014; [g]Kreipe and Palomaki 2012; [h]Norris et al. 2014; [i]American Psychiatric Association 2000; [j]Sokol et al. 2002; [k]American Psychiatric Association 2013; [l]Strober 1995; [m]Halmi et al. 2005.

AN, anorexia nervosa; PANDAS, pediatric autoimmune neuropsychiatric disorder associated with streptococcal infections; ARFID, avoidant/restrictive food intake disorder; PANS, pediatric acute-onset neuropsychiatric syndrome.

Palomaki 2012). In addition, food neophobia, the avoidance of trying new foods, was not found with our cases, as prior to the onset of illness our patients consumed typical diets with a variety of foods (Dovey et al. 2008). As with all psychiatric diagnoses, a medical condition must be ruled out as the primary cause of the symptoms. Comorbid medical conditions with ARFID and eating disorder-like presentations would include gastroparesis, low oral muscle tone or coordination, dysphagia, achalasia, esophagitis, and irritable bowel syndrome. Other potential causes of presenting symptoms include food allergies and occult malignancies.

Conclusions

Eating disorders in children are on the rise, and the burden of these disorders on the healthcare system is high. Between 1999 and 2006, there was an 119% increase in eating disorder-related hospitalizations for children < 12 years of age, per an analysis performed by the Agency for Healthcare Research and Quality (Rosen 2010). In particular, the steep rise in males with eating disorders is of concern (Carlat et al. 1997; Rosen 2003; Dominé et al. 2009). We hypothesize that the rise in eating disorders in young children, especially in males, as suggested by our cases, may be linked to a PANS presentation that could be missed by clinicians. It is noteworthy that there exists a preponderance of males with pediatric OCD (Geller and March 2012) as well as PANS (Swedo et al. 2012); the male preponderance seen in our sample may simply reflect what has been described for pediatric OCD. It is our hope that a PANS diagnosis will be considered in children who develop acute-onset food avoidance or restriction. The management and outcome of children with a PANS presentation differ from those for AN and ARFID, as treatment with antibiotics or immunomodulatory therapies is often curative (Perlmutter et al. 1999; Murphy and Pichichero 2002; Snider et al. 2005; Murphy et al. in press), as in the cases described above.

Clinical Significance

The cases described in this series demonstrate clinically important differences between the disordered eating of PANS and that of ARFID or AN. Acuity of onset, male prevalence, and young age at presentation are the most striking differences, and serve to distinguish the PANS patients from others with eating disorders. In the PANS group, environmental factors, particularly GAS infections, can lead to a cascade of immunological, psychological, and physical symptoms that result in abrupt restriction and/or aversion to food. Early appropriate diagnosis and treatment of PANS is essential, as prompt treatment with antibiotics or immunomodulatory therapies can produce dramatic symptom improvements. Further research is required to determine the best treatment practices for disordered eating in the PANDAS/PANS cohort.

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