Review Article

Obsessive-Compulsive Spectrum Disorders in Childhood and Adolescence

Ola Omar Shahin
Department of Psychiatry, Cairo University

ABSTRACT

Over the last decade studies conducted on children and adolescents with Obsessive- compulsive disorder (OCD) both in clinical setting and in the community shown that the specific features of OCD are essentially identical in children, adolescents and adults However, in children and adolescents the disorder is accompanied by a wide range of co morbidity, including mood disorder, anxiety disorder, learning difficulties and or tic disorder. In recent years body of data has supported the notion of an obsessive-compulsive spectrum disorder. Is based on similarities among disorders across several domains including symptomatology, associated clinical features possible etiology, familial transmission and response to selective pharmacological or behavioral treatment. Several approaches have been put forward each based on a rather different framework. Overlaps exist among these approach indicating that the neurobiology of OCD and related disorders is increasingly consolidated. **(Int. J. Ch. Neuropsychiatry, 2004, 1(1): 1-20)**

INTRODUCTION

Over the last decade studies conducted on children and adolescents with obsessive-compulsive disorder (OCD) both in clinical, setting and in the community shown that the specific features of OCD are essentially; identical In children adolescents and adults It is a disorder of heterogeneous origin with symptoms that are considered to be distressing, time consuming and functionally impairing It is frequently associated with severe disruption to academic performance, peer relation ship and family functioning.[1] However, in children and adolescents the disorder is accompanied by a wide range of co morbidity including mood disorder, anxiety disorder learning difficulties and or tic disorder.[2]

In recent years, obsessive-compulsive spectrum disorders (OCSDs) have emerged as a differential entity characterized with intrusive thoughts or repetitive behavior whose major syndrome would be the classical compulsive disorder The concept is based on similarities among disorders across several domains including; symptoms, associated clinical features (age of onset, clinical course and co morbidity) possible etiology, familial transmission and response to selective pharmacological or behavioral treatment.[3]

Several approaches to the spectrum of obsessive-compulsive spectrum disorder have been put forward each based on a rather

different framework. Overlaps exist among these approaches indicating that the neurobiology of OCD and related disorders is increasingly consolidated.[4]

Symptom Profile

The clinical phenotype and diagnostic criteria for OCD are similar in children and in adults. Obsessive-compulsive disorder is characterized by a range of obsessions that are defined as recurrent persistent thoughts, disturbing ideas, impulses and images as well as compulsions that are ego-distonic intrusive and senseless repetitive behavior performed according to certain rules or in a stereotyped fashion that the person feel driven to perform in response to obsessions, designed to reduce discomfort.[5]

OCD is characterized by either obsessions or compulsions. Compared to adult onset type. However, it was demonstrated in one study that 30% to 50 % of OCD children have poor or little insight regarding their disorders.[6]

Obsessions in juvenile OCD are more likely to be focusing on contamination and cleaning. Rituals such as; washing, checking, repeating, touching, checking and counting are the most common in children. They are not required to recognize that obsession or compulsions are excessive or unrealistic. Rituals in the form of washing, checking, repeating, touching, counting, are the most common in children who tend to change their principle symptoms over time.[2]

OCSDs share with OCD important diagnostic symptom profile. It occurs in a variety of psychiatric and neurological disorders. The obsessions may be in the form of preoccupation with the body (body dimorphic disorder) preoccupation with body sensation (depersonalization), preoccupation with body weight (anorexia nervosa), or preoccupation with body illness, (hypochondriasis). Rituals may be in the form of stereotyped motor or grooming behavior (Tourette's disorder, Trichotillomania, onychophagia, face picking) or driven forces of impulse control (pathological gambling, sexual compulsions, addiction, borderline personality disorder). These common features suggest an overlap between OCD, eating disorder, impulse control discords, somatoform disorders and neurological disorders.[7]

OCSDs can be conceptualized and consisted of 3 distinct symptom clusters; the first cluster includes disorder of impulse control (intermittent explosive disorder, pyromania, kleptomania, pathological gambling, Trichotillomania, paraphillias, sexual impulsion, and sexual acting out behavior. These are characterized by pleasure producing behavior irrespective to the painful sequences. They are also accompanied by a high tendency for risk seeking behavior, defect in harm avoidance, and little anticipatory anxiety.[1]

The second obsessive-compulsive symptom cluster is characterized by an exaggerated preoccupation with appearance, weight or body sensation as in the case body dysmorphic disorders, eating disorders and depersonalization disorder.[7]

The third symptom cluster includes neurological disorders with repetitive behaviors such as; Autism, Asperger's disorder, Tourette's syndrome, Epilepsy and Sydenham's chorea.[8]

On the basis of shared clinical and phenomenological features, age of onset, and course of illness, co morbidity, family history and sometimes responsiveness to treatment several disorders have been suggested to be

included as OCSDs. These disorders may prove to share common neurophysiological or biological substrates and possible related genetic transmission.[9]

Associated Features

Co morbidity:

Studies of juvenile OCD have indicated that co morbidity is the rule where as OCD as an only diagnosis is the exception in children and adolescence. The overall lifetime co morbidity has been shown to be as high as 75%[10].

At least 2/3 of juveniles with OCD will have one or more additional axis I diagnosis. Juvenile OCD is characterized by the presence of high rates for co morbid disruptive behavior disorders, specific developmental disorders and enuresis .As many as 1/3 lo 1/2 of children with OCD has a current or past-history of another anxiety disorder. Overanxious and separation anxiety appear to be the most frequent in children. Panic and generalized anxiety is the most common in adolescent.[11]

Co morbid conditions appear in chronological sequences with attention deficit hyperactivity disorders, specific developmental disorders, anxiety disorders and Tourette's disorder, often occurring years before the onset of OCD symptoms.[2]

Using the minimal exclusion criteria in a study conducted on juvenile OCD, co morbidity was found in 69% of the sample. 22% were diagnosed with disruptive disorder, 20% with mood disorder, 19% with anxiety disorder and 17% with tic disorders.[12]

The presence of schizophrenic spectrum disorders in families of OCD children may hinder the response of OCD children to treatment.[2]

Distinctive patterns of co morbid disorders in pediatric obsessive-compulsive disorders have implications of pharmacological treatment in OCD youngsters. It makes the management more challenging.

Dimensional Approach

Obsessive - compulsive spectrum disorders can be viewed along a-continuum with overestimation of harm on the compulsive end and underestimation of harm on the impulsive end. Disorders of compulsivity include disorders like body dysmorphic disorder, anorexia nervosa and hypochondriasis. Disorders characterized by substantial impulsivity, include; disorders of impulse control such as Trichotillomania Kleptomania and Paraphillias. This dimension may be hypothesized within a biological framework of hyperfrontality and increased Seretonergic sensitivity associated with compulsive disorder and hypofrontality with reduced presynaptic Seretonergic sensitivity i.e. reduced activities of these variables, on the impulsive group disorder.[13]

The difference between the two lies in the driven loci of action, where in compulsivity it is to decrease discomfort and alleviate anxiety associated with rituals while in impulsivity it is to obtain gratification and to illicit pleasure. Both may be present in the same individual and the common inability to inhibit or delay an action or a repetitive course of the illness.[7]

As regards the number and severity of the symptoms, obsessive-compulsive phenomena appear to be a continuum with few symptoms and minimal severity at one end and many symptoms with severe

impairment on the other end. Obsessive-compulsive symptoms may occur in the context of OCD symptoms or the symptoms may appear scattered or distributed as symptoms among other psychiatric disorder.[14]

Etiology:

It is known that OCSDs are heterogeneous group of disorders. It is probably multifactorial in terms of pathophysiology. Environmental factors, genetic factors and neurobiological factors have been cited as possible aetiological factors in this group of disorders.[2]

I. Genetic Factors and Family Studies:

The familial nature of OCD has been observed since 1930 and both Freud and Janet thought it is likely that constitutional or genetic factors 'were important in the pathogenesis of the disorder.[15]

Genetic factors and family studies have been cited as possible etiological factors in OCSDs. A genetic susceptibility for OCD is suggested by the familial links between OCD and Tourette's disorder. The family genetic data in conjunction with twin findings suggested that, chronic multiple tics and some cases of obsess ional disorder may constitute different manifestations of the same genetically determined disorder.[16]

Children with OCD and TS tend to show an elevated level of either disorder reported in 1/3 of first-degree relatives suggesting a bi-directional relationship. Also, prevalence rates of OCD and tic disorders were significantly greater among, 1st degree relatives of OCD, than among relatives of unaffected subjects.[17]

It seems that the genetic vulnerability can produce a vastly different phenotype genes. The genes do not code for a behavior or even a spectrum of behavior. They code for proteins that are expressed in specific cells in specific brain region in a regionally specific fashion, producing the predisposition to the specific behavior that gives the different variation in phenotypes. TS, OCD and ADHD could be related in this way to TS gene product in brain region. It provide clues for their shared neurobiological substrate which in turn is not identical because these disorders are phenomenological distinct and this in turn must be brain based.[18]

OCD seems to be increased in the first-degree relatives of children and adolescents with trichotillomania. It appears that most youngsters with this condition do not have other obsessive-compulsive symptoms.[19]

Family studies of cases with OCD were found to be; highly correlated with body dysmorphic disorder. The first-degree relatives of juvenile OCD probands show high rate of mood disorder anxiety disorder, OCD, ADHD and tic disorder.[17]

Autism has been associated with OCD spectrum on the basis of high rates of OCD in the1st degree relatives of autistic probands.[9]

II. Organic Factors:

The biological model of OCSDs, was first suggested by, the association of OCD with the neurological insults and diseases. Clinical studies demonstrated the presence of adverse neurological and perinatal events in childhood OCD. Seizure disorders, head trauma, cerebral hemorrhage encephalitis and multiple sclerosis have been reported.[20]

Numerous brain insults resulting in basal ganglia damage e.g. head injury, brain tumor, and carbon monoxide poisoning has been reported to be related to the onset of OCD. Patients with known basal ganglia illness including post-encephalitic Parkinson's

disease and Huntington's chorea have an increased rate of OCD symptoms.[21]

PANDAS: Perhaps the most exciting work in the field of OCD is the relationship between OCD and Sydenham's Chorea (Neurological version of Rheumatic fever). The incidence of obsessive-compulsive symptoms is increased in pediatric patients with Sydenham's chorea. It is an autoimmune response of the basal ganglia caused by misdirected antibodies from a streptococcal infection. A new syndrome termed "Pediatric Autoimmune Neuro-psychiatric Disorder" (PANDAS) is associated with group A, B, haemolytic Streptococcal infection (GABHS). It is defined as an autoimmune subgrouping calling for immunomodulatory treatment. It is characterized by prepubertal onset of OCD, tic disorders, hyperactivity or choreoform movement. This group of PANDAS likely represents a genetic vulnerability different from a late onset OCD.[20]

The validity of this syndrome is supported by the associated leucocyte marker is known to be related to rheumatic fever, and detection of antineuronal antibodies D8/17 in peripheral blood. Several children with sudden onset of OCD Symptoms that was triggered by GABHS infection have fear of eating, as a prominent obsession reported, stressing the associated severe loss of weight within a short period of time from the onset of OCD symptom. This may support the proposal of OCD and anorexia as spectrum disorder.[22]

III. Neurochemical Dysfunction:

A) Serotonergic Model:

The Serotonergic model of OCD followed the discovery of relative efficacy of selective Serotonine reuptake inhibitors (SSRIs). Considerable evidence implicates Serotonergic dysfunction in the neurobiology of obsessive propulsive spectrum disorders.[23]

Serotonergic pathway plays an important role in compulsive and impulsive disorders. Compulsive disorders arc always associated with increased frontal lobe activity and increased sensitivity of specific Serotonine receptor subsystem. In contrast, decreased frontal lobe activity and decreased presynaptic function may underline the impulsive disorder.[13]

Serotonergic (5 HT) function may be measured by cerebrospinal fluid metabolite 5 Hyroxy-lndole Acetic Acid (5HIAA); by behavioral and endocrinal response to Serotonergic probes as m-CPP, and by treatment outcome to Serotonin reuptake blockers (Fluoxetine, clormipramine, Fluyoxamine, and others).[7]

Acute Serotonergic challenges in OCSDs also show irregularities in 5HT function. Patients with compulsive impulsive disorders may demonstrate opposing behavioral response to 5HT agonist mCPP. Compulsive disorders, such as, anorexia nervosa, OCD, and Tourette's disorder tend to report blunted prolactin response. They show dysphoria and increased obsessional thoughts and compulsive urges On the other hand patients with impulsive behavior such as Trichotillomania,and pathological gamblers demonstrated increased prolactin response to challenge with mCPP.They do not show dysphoric response. The partial agonists mCPP has been reported to produce symptom exacerbation and Prolactin and Cortisol abnormalities in OCD patients [Hollander et al., 1993]. Although these results are not always replicated, mCPP act as an agonists at 5HT1 receptor site, as an antagoinst at 5 HT3

and a mixed agonists and antagonist at 5HT2 receptor site. Platelet monoamine oxidase peripheral indicator of serotonin function was also lowered in impulsive disorders.[13,8]

Other compulsive disorders such as anorexia nervosa, showed an increase 5 HIAA overall or in subgroups of patients responsive to 5HT reuptake blockers. Patients with bulimia nervosa have been reported to have persistent disturbance of brain 5HT activity and frequently benefit from SRI treatment.[24]

Patients with impulsive aggressive and violent suicidal behavior have decreased levels of CSF 5HIAA. Patients successfully completing violent suicide also have decreased 5 HT receptors in frontal region.[7,8]

Compulsive and impulsive disorders seem to have a different dysregulation in Serotonin pathways, which may explain differential response to SRI treatment (longer therapeutic lag and higher dose response in compulsive disorders and rapid response that tends to diminish with time in impulsive disorders)[1].

B) Dopaminergic Model:

It is unlikely that the neurotransmitter, dysregutation can be attributed to just one system. It is possible that the volume reduction in the basal ganglia may account for elevated levels of presynaptic transporter, postsynaptic D2 receptor and DOPA-decarboxylase that have been reported in Tourette's syndrome. Increased D2 receptor level in Caudate nucleus may suggest the dopaminergic involvement. In a study using PET with tracer F18 flurodopa in Tourrette's disorder was associated with accumulation of f DOPA in synaptic terminal in the left caudate and right midbrain which provides evidence for dopaminergic dysfunction in Tourette's disorders.[25]

Support for the role of altered dopaminergic functioning comes from she clinical observation that neuroleptics such as Haloperidol and Pimozide, which preferentially block central dopaminergic D2 receptor, partially suppress tics in most patients where as dopaminergic agonist such as L-dopa exacerbate tics.[26]

Now, there are a whole host of childhood neurodevelopment disorders for which evidence is rapidly accumulating to suggest dopaminergic pathway involvement. These disorders include Lesch Nyhan disease, Autism, ADHD, and Tourette's disorder. The remarkable number of disorders and the striking differences in phenotypes suggest not only the importance of dopaminergic system to the normal conduct of, motor, cognitive and emotional functions but, its vulnerability.[25]

C) Glutametergic Neurotransmitters

MRI studies have shown elevated glutametergic concentration (glutamate/ glutamine, GABA, G1X) in the caudate nucleus of pediatric patients with OCD compared to normal control. Following SSRI treatment for 12 weeks the level of the glutametergic concentration in the caudate nucleus decrease in patients with OCD associated with reduction in OCD symptoms. Glutametergic Serotonine modulation may be involved in the pathogenesis of OCD.[27,28]

Neurobiological Findings

Recent studies using functional and structural neuroimaging in youngsters with OCSDs together with neuropsychological studies revealed the existence of defects in

the frontal orbital basal ganglia thalamus cortical and their limbic connection.[3]

Structural abnormalities, using CTS and MRI, showed increased ventricular brain ratios in OCD adolescents compared to control, with decreased volume of caudate and increased third ventricle volume in children with OCD. MRI demonstrated increased size of genue of corpus callosum, that was positively associated with the severity of OCD[29]. There was also small striatal volume in pediatric OCD patients that was negatively correlated with the severity of symptom It might be related to increased myelinization of fibers in that area. The basal ganglia appear to play a crucial role, through their extensive connection to sensorimotor and associated cortex, integrating sensorimotor information and motor control.[27]

Pediatric patients with Sydenham's chorea showed selective anatomic basal ganglia abnormalities similar to finding present in OCD pediatric patient.[29]

CT and MRI on female adolescents with either anorexia nervosa or bulimia nervosa revealed reduction of both total white and grey mater volume with enlarged lateral ventricles and cortical sulci that are strongly related with weight loss. MRI also reported reduction in subcortical region mainly in size of thalamus and midbrain. This reduction is more in anorectic than in bulimic patient.[30]

PET studies demonstrated increased glucose metabolism in orbitofrontal cortex in OCD patients. Moreover SPECT have documented increased blood flow in the frontal region with decreased blood flow in the head of caudate.[7]

Functional abnormalities have been demonstrated in other OCSDs. PET and SPECT revealed hyperfrontality with hyperperfusion to be associated with compulsive disorders, while hypofrontality and hyperperusion were reported in impulsive disorders Anorexia nervosa is associated with right posterior hypometabolism, right anterior hypermetabolism and right-sided abnormal EEG .Notably impulsive patients such as those of borderline personality have decreased frontal glucose metabolic rate.[13]

SPECT study involving children with anorexia nervosa showed an abnormal degree of temporal lobe asymmetry. This may reflect an underlying primary cerebral abnormality in the limbic system that has clear connection with frontal and temporal lobe and hypothalamus. It links the disturbance to the cortical function, emotional response and appetite control.[30]

Developmental Perspectives

Freud, Piaget and others have noted the ubiquitous repetitive activities and rituals that characterize the daily behavior of young children. Some represent a pleasurable exercise for serialization and categorization, others serve to reduce anxiety by reinforcing object constancy at times of separation or uncertainty. Still others may ward-off potentially dangerous impulses.[31]

Developmental studies found that obsessive concerns about symmetry or order and obsessive insistence on sameness are very common in preschoolers. When they persist beyond age 4 to 5 years they are considered to be associated with poor adaptation and increased level of parental obsessionality. In later childhood formalized games, hobbies and collections are common and promote social interactions.

Therefore it can be considered as an indirect method for reducing tension of

anxiety, needs of solving problems, substituting permissible satisfaction for taboo-ones, increasing reward from and acceptance by other persons or avoiding punishment and deprivation. The reason why they fail as adjustive techniques is that they offer transient tension- reaction. External boundaries of the disorder are permeable with a large degree of overlap with other psychiatric disorder and an association with certain neurological disorders.[32]

Psychoanalytic Perspective

Freud slated that the obsession & compulsions might be classified into one of opposite categories. They may be of a negative and defensive character as prohibitions, precautions and expectations or more positively; they may symbolically, and in a disguised form provide substitute gratification of " Id " impulses.[33]

The psychogenesis of OCD lies in the disturbance in normal growth and development related to anal - sadistic phase. Normally the impulses associated with anal-sadistic phases are modified in the Oedipal and succeeding stages of development. If however a disturbance occur in this developmental process, unmodified anal-sadistic impulses remain as components of the individuals psychological make-up. Ordinarily these impulses will be controlled and disguised by character traits and may not significantly affect the individual function in the ordinary course of daily living. They remain however as fixation points, which may under certain circumstances give rise to difficulties. These factors along with employment of specific ego defenses (isolation, undoing and displacement) combine to produce the clinical symptoms of obsession, compulsion and compulsive acts.[34]

Hierarchical Analysis of Obsession

The concept of obsession is complex and therefore lends itself well to the general type of Hierarchical analysis suggested by Herbert Simon (1962). Obsession is explained through at least 3 conceptual frameworks. The 1st defines obsession in term of basic behavioral dimension of repetitiveness. This dimension alone captures all manners of repetitive phenomena (e.g. preservation-tics) and hence has high sensitivity. The 2nd level includes subjective qualifiers such as resistance, feelings of interference, slowness, indecision and paralysis. These increase the discriminating power of concept, but are not good enough to exclude clinical phenomena such as the forced thinking of epilepsy or the repetitious and transient compulsive behavior of brain-damaged patients. The 3rd level includes criteria such as insightlessness, prototypical contents involving violence, dirt, sex, religion ...etc.[34].

Epidemiological Studies

Prevalence:

Childhood OCD is a chronic and not uncommon psychological condition with lifetime prevalence estimates 1-3%. Retrospective studies with adult OCD patients suggested that 30 to 50% of them had onset of their symptoms during childhood or adolescent Intrusive images 6%, disturbing thoughts 8%, hoarding 29%, repetitive actions 27%, urges to repeat 49%, and extreme neatness 72%. Only 3.5% of those regard their symptoms as always

distressing, Subclinical OCD in adolescents was found to range from 4% to 19%.[35]

The frequency of OCD in clinical samples of children is generally lower than those Found in the community. This discrepancy may be due to the fact that children's ritualistic activity tends to be considered as part of the normal developmental behavioral repertoire throughout the life span.[36]

The international reports show a prevalence rate of 4.1% in Newzeland with equal gender ratio and comorbidity with other psychiatric disorder in 75% to 84%. In a two stage epidemiologic study in southeastern US reported a life lime prevalence rate of juvenile OCD of 3% and a 1-year incidence of 0.7%.[37]

2-4% of adolescents in the community samples meet full DSMIV criteria of OCD, other youngsters lend to have obsession and compulsions that tail to meet the criteria by virtue or by being reporting symptoms that are less disturbing impairing or time consuming. The prevalence of obsessive-compulsive symptom was found to be 2.1% for females and 2.2% for male.[39]

In an Egyptian study for OC symptoms in adolescents, school students had a higher prevalence of OC symptom (38.7%) compared to university students (32.7%). 83.3% of OC positive symptoms were in 1st order child. Positive consanguinity and family history of psychiatric illness had higher incidence in school students. Aggressive obsession, contamination, and religious obsessions as well as cleaning, washing, checking and repeating compulsions were significantly higher in the younger students. OCD was diagnosed in 19.6 % of those with positive OC symptom with higher presentation in male group.[14]

In an Egyptian study concerning obsessive manifestations and symptoms in children attending psychiatric clinics, it was found that the most prevailing obsessions were contamination and self-injury and was highly comorbid with depression and anxiety. The most common rituals were Hand washing, ordering, touching and counting.[40]

Reports concerning the actual incidence of bulimia nervosa as a clinical diagnosis in a community sample found it to be less than 1-2% in children, while that for anorexia nervosa was 0.1-0.2%.[30]

Community survey found that as many as 13% of boys and 11 % of girls are reported by their parents to have tics[31]. The prevalence of body dysmorphic disorder is 0.1-1.0%. Co morbidity with OCD may be up to 38%.[8]

The lifetime prevalence estimates of the full syndrome of classical autistic disorder are 2-5/10000. Symptoms typically present by the age of 3 and often begin in infancy.[1]

Age:

Although the OCD can start as early as two years, but still there is an increase incidence in the teenage and early adult years. The obsessive-compulsive related disorders usually have an age of onset in late adolescents or in the early twenties. There is a lag between the onset of illness and clinical presentation. Thus, OCD appears to have a bimodal peak of incidence. Body dysmorphic disorders often present in late adolescence to early twenties. Pica starts as early as 18-24 months and, declines sharply after 3 years of age. Anorexia usually starts as early as 8 years of age up to 30 years with bimodal peak at 13-14 and 17-18 years. Until recently, very few cases of bulimia below the age of 14 years were reported, with rare cases under the age of 12 years.[8,30]

Tics are common among children, with the highest apparent prevalence in children between 7 and 11 years. The initial symptoms of Tourette's disorder most frequently appear in pre-puberty from ages 5-10 years. Initially, they may resemble transient motor tics of childhood in being mild and transient involving the face, head and upper extremities.[31]

Sex:

In contrast to adult OCD patients who demonstrate either equal gender representation or a slight preponderance in boys, pediatric clinical OCD patients show a male to female ratio of approximately 3:2. The juvenile-onset type with common presentation in males may represent an etiologically distinct disorder[11].

There is a difference concerning sex in Juvenile OCD subjects but still spectrum related disorders tend to differ with respect to gender.[8,23]

The prevalence of obsessive traits in a sample of Egyptian students was found to he 262% and that of OC symptoms was 43 1% Obsessive-compulsive symptoms were more prevalent among the younger female students in first-born subjects. Aggressive obsessions, fear of contamination, religious obsessions and cleaning compulsions were the commonest among the sample. 19.6% of the subjects fulfilled the ICD criteria for OCD.[14]

Prevalence of bulimia nervosa in female adolescents reached 4% in a US study.

Impulse control disorders are equally expressed in both sexes. Females tend to pull their hair and injure themselves while males are more likely to explode, set fire and act out sexually[40].

Females are over presented in body dysmorphic disorders, compulsive bings and Kleptomania. Males seem to predominate in tic disorders, pyromania and hypo-chondriasis[4]. It is not clear whether the differences are due to endocrinal, neuroantomical or sociocultural Factors.[13]

Theoretical & Clinical implication of OCSDs

Obsessive-compulsive spectrum disorders, overlap with many distinct psychiatric entities. Some of these disorders will be presented.

Feeding and Eating Disorders

It has been suggested that eating disorders belong to obsessive-compulsive spectrum disorders. Symptoms related to food, weight, body image or exercise frequently share the characteristics of obsessions or compulsions. In addition, eating disorder patients may exhibit the full range of obsession and compulsion including; pathological doubt, symmetry and contamination worries، repeating, checking and grooming[10].

1) Rumination

This rather rare condition is defined as the repeated voluntary regurgitation of gastric contents without associated nausea or G.IT disorder. It is encountered predominantly among children. The onset is usually within the 1st year of life. First it was called "Psychogenic rumination"; it is associated with significant disturbance of mother-child relationship and occurs among children with normal development. It is relatively rare and is associated with medical complications. Also, the mother who fails to feed the child who persistently ruminates. Her

failure may render the feeding act aversive. Successful feeding needs reparation of oral motor function and reflex closure of vocal cords whose component is based in the sub -cortical level.[41]

2) **Pica:**

Is the compulsive eating of non-nutritive substances and can have serious medical implication. Il is more common in women and in children II is probably a behavioral pattern driven by multiple factors some recent evidence supports including pica with obsessive-compulsive spectrum disorders It is either due to nutritional deficiency or inadequate mother-child relationship producing inner oral needs that are expressed in this feeding habit.

It may be seen in children with MR, pervasive development disorder and Klien Levin syndrome. It is said that 62% of mothers of children with pica have pica themselves. Other associated compulsive acts such as thumb suckling and nail biting this is to be interpreted as a distorted form of instinctual seeking of gratification and a defense against loss of security and lack of parental availability.[42,43]

3) **Anorexia nervosa:**

It has been classified in DSM-IV as an eating disorder characterized by disturbed body image, obsessive fears of being fat, and compulsive driven attempts to reduce weight via restricted eating, abuse of laxatives, and or diet pills or excessive exercise. In children, weight is controlled through food avoidance self induced vomiting and excessive exercise dial are mostly carried out secretly the onset of anorexia is usually between 12-15 years. Typical characteristics of anorectic patients include, impulsive outbursts, ambivalence and compulsiveness. Intellectual superiority and, is common in this group of patients characterization by the family as strong-minded stubborn determined individuals.[5]

Anorexia and OCD often overlaps clinically and neurobiological. Anorexic subjects demonstrated higher scores on Yale Brown obsessive-compulsive scale independent from the eating disorder obsessive thoughts recorded include fear of not doing something right, the need for symmetry, exactness order and the fear that something terrible could happen. The lifetime prevalence of OCD in patients with anorexia has been estimated to be 28%. There is increased ratio of co morbid or prior anorexia in population with OCD.[24]

4) **Bulimia nervosa:**

Recurrent episodes, of Bing eating in, which a number of behaviors such as, feeding and impulse control are poorly modulated. It is associated with recurrent inappropriate compensatory behavior to prevent weight gain[5]. Loss of control with over-eating occurs intermittently or typically after the unset of dieting behavior they tend to have extremes of self-control so that the impulsive and compulsive behavior is common. Very few cases have been reported below 14 years of age and relatively rare in children below 12 years of age. A failure to have a meaningful relationship is reported[45].

Young patients with anorexia nervosa and bulimia nervosa require comprehensive treatment approach that

ideally involve pediatric or adolescent medical supervision, behavioral 'management, family therapy and often psychopharmacologic treatment. An alliance between mental health and medical personal which is usually best achieved in specialized programs for eating disorders.[30]

Impulse Control Disorders:

Disorders of impulse control are characterized by impulsivity or aggression and lack of control. Affected individuals drive pleasure arousal and gratification from their impulsive behavior. Males and females can both express impulsivity but they do so in different ways. Males are more likely to gamble, explode and set lire. Females are more likely to pull out hair[40].

1. Trichotillomania (TTM):

Trichotillomania is classified in the DSM-IV as an impulse control disorder that is characterized by an irresistible urge to pull out one's hair accompanied by a building of tension and a subsequent sense of relief. The hair pulling is usually ego dystonic and may result in extensive disfiguring hair loss. Average age at onset is 10.6 years. Child behavioral profile of hair pulling strongly resembles that OCD. There is a debate over this classification as trichotillomania presents compulsive as well as impulsive features.[19,45]

Compulsive features are suggested by similarities in phenomenology and neurobiology. These include inability to inhibit repetitive ego dystonic behavior, higher co morbidity between the two disorders than might be expected by chance. They tend to commonly have parental history of tics, habits or OCD symptoms[31]. Girls are more affected than boys; this differs from that of OCD children, which shows either affection of girls and boys or a higher prevalence for males[11].

Impulsive features include features of pleasurable feeling following symptomatic behavior. The high rate of personality disorders in some studies and the patterns of Serotonergic function are consistent with impulsive disorders some patients reported pleasure on hair pulling.[20]

To explore a possible relationship between trichotillomania and OCD. The first-degree relative of 16 female proband with chronic TTM were compared with control group for OCD and TTM. There was a trend for a higher rate of OCD in TTM families which is consistent with the concept OCD spectrum that included TTM and other pathologically grooming behavior.[7]

Until recently, little was known about the effective treatment for TTM. Trials by SSRIs, fluoxetine and clomipramine proved effective in some cases. The serotonergic antidepressants have minimal impact on these behaviors in juvenile patient. Comorbid depression is common a medication may be otherwise helpful. Behavioral treatment is often the treatment of choice for these patients.[19]

2- Onycophagia (Nail-Biting):

It is unwanted behavior of childhood-onset. It has been associated with OCD. It is usually common among children and adults. It is usually an expression of anxiety. As with all other body manifestation, it is primarily a symptom

of deep underlying disorder. It is usually generated by intense, hostile or competitive impulses towards a person. To resolve this conflict, the patient bites his nails, thus denies his hostility, injure him and demonstrate his punishment. Behavioral therapy may help. It is shown to respond specifically to pharmacological treatment with Serotonergic agents[45,19].

3. **Temper Outbursts:**
   Here the child works himself into a rage. Stamping his feet, throwing himself to the floor, striking, kicking, screaming and crying. It may be associated by, head banging. Il is a type of attention seeking to get his way when parents do not comply immediately with his wishes and needs. It is an attempt to avoid anticipated punishment. Sometimes it is a compensation of low self-esteem and a desire for punishment due to poorly word-off guilty feelings[45].
4. **Kleptomania:**
   Kleptomania is characterized by an irresistible impulse to steal objects not needed for personal use or for their momentary value. Kleptomania is related to obsessive-compulsive spectrum disorder and affective spectrum disorders. In OCSDs neuroimaging &neuropsychological tasks have revealed abnormal functioning in the frontal brain which also could he related to kleptomania. Consolidated findings from animal and human studies have implied central Serotonergic transmission in the genesis of OCSDs disorders and affective spectrum disorders. These results suggest that kleptomania like other disorders of the above mentioned spectrum could have an abnormality in Serotonergic transmission in common. Several recent case reports have shown that Serotonin specific reuptake inhibitors could be effective in the treatments of kleptomania. It thus supports the assumption that this syndrome involves a dysfunctional Serotonergic mechanism as it is another obsessive compulsive spectrum disorder[46].

Tic Disorders:

The cluster of disorders included simple, transient or chronic motor or vocal tics. It also include complex moloi and vocal tic(Tourette's syndrom). The stereotypic movement involved in these disorders originates from the basal ganglia. Those individuals display both obsessive and compulsive behavior.

Tourette's Syndrome:

It is more common disorder that represents the most complex and severe manifestation of the spectrum of tic disorders. It is a sudden motor stereotype complex tics that is associated with compulsive phenomena. Evidence indicates that it is a chronic familial disorder with long-term generally favorable outcome. Tourette's syndrome is characterized by motor and vocal tics, which are defined as sudden repetitive movement, gestures or utterances that typically mimic normal behavioral sequences[5] 30-40% of Tourette's syndrome patients have some obsessive-compulsive features. Moreover many Tourette's patients feel need to perform tics until they are completed or "Just right"[19].

MRI studies in children showed basal ganglia dysfunction with with reported

abnormal sized of the basal ganglia on the left side and left putamen and reduction in right caudate in more severely affected probands. Visual spatial dysfunction similar to that found in OCD have been reported in Tourett's patients.[31]

Abnormalities in dopaminergic innervations in caudate and striatum nucleus have been strongly implicated in Tourette's syndrome. Abnormal activity of Dopa decarboxylase may reflect a variety of functioning elements of the dopamine system. Increased D2 receptor level in caudate appear to account for some of the non-genetic determinants of variance in symptom severity. The hyperinnervation by dopaminergic receptor would over determine through multiple effects or the phenomenology of TS related conditions as, recurrent obsessional thoughts compulsions and impulsive behavior depending upon which portion of the striatlal ,pallidal or thalamic nuclei is disinhibited[18]. Serotonergic dysfunction is also suggested. In OCD patients with tics the ratio of Serotonergic (CSF-5H1AA) versus dopaminergic (HVA) measures was higher than that in OCD patients without tics[19]. SSRIs have been reported to decrease OC symptoms associated with Tourette's but not the tics themselves. However, neuroleptic addition to SSRI is helpful in treatment of OCD with history of tics[7].

Pervasive Developmental Disorders:

Autism:

It is a pervasive developmental disorder characterized by three core components; social deficits, speech and communication impairment and repetitive behavior with restricted interest[5].

The lifetime estimation of classical autistic disorder is 2-5 per 10,000. The onset is typically by the age of 3 years. The first identifiable impairment is that of social skills that can be observed as early as 6 months of age[13]. The stereotyped complex hand and body movement and repetitive behavior seen in autistic syndrome may be easily described as obsessive compulsive symptom but seems different in nature. Autistic children usually lack insight in their behavior. A high rate OCD is found the 1st degree relative of autistic children.[9,21]

Some studies in whole blood and in plasma suggested an elevation of Serotonin in some autistic children. Relatives of autistic probands, with high Serotonin level,was found to be, rated high on scales of anxiety, depression and OCD. Thus, blood Serotonin levels may be familial and possibly associated with genetic liability to specific subtypes of autism[8]. Decrease in Catecholamine and related metabolites and an increase in dopamine metabolite HVA in CSF in autistic proband which can be associated with increased stereotype and social impairment.[13]

There is as well increased expression of ß cell autoimmune marker D8/17 that is significantly related to repetitive behavior in autism. The involvement of high Serotonin level associated with repetitive behavior and OCD disorder in 1s1 degree relatives of autistic disorder in addition to the expression of ß cell cell autoimmune marker that was proved to be present in OCD proband with response to SRI, supports the classification of autism as an OCSDs.[8]

SPECT studies revealed autism to be associated with hypoperfusion in the left hemisphere involving sensory motor and language areas Left temporal lobe

dysfunction was suggested. Others stressed the impairment to be in right hemisphere dysfunction responsible for impairment in communication and monotonic prosody and paucity of gestures.[31]

Currently, no medication has been established for the treatment of autism. Some are used to treat the core symptoms, current psychiatric disorder or associated medical disease. SSRI seem promising in improving global severity and dimensional deficits in autism including; compulsive, obsessional symptoms, involuntary movements and some social and language deficits. They do not have the seizure or cardiac risks associated with Clomipramine.The most effective treatment seems to be a multi-modal approach involving behavioral pharmacological, psychotherapy family and vocational therapies.[1,8]

Somatoform Disorders:

Body Dysmorphic Disorder (BDD):

This disorder is characterized mainly by an excessive concern with imagined or over valued defects in bodily appearance. Areas of concern focus primarily on the face and head but can also include feet hands and sexual body parts.In juvenile patients, these somatic obsessions may represent the only symptom. It is more common in adolescents than in pre-pubertal children and may present with preoccupation and dissatisfaction with hair-style leading to grooming behaviors and excessive mirror checking, repeated request for reassurance and avoidance of social situations for fear of exposing the perceived defect.[8]

Prevalence of BDD is 0.1 to 1% of the population and co morbidity with OCD may reach up to 38%. Family history of OCD was also found to be high in families of BDD. This in addition to similarities in clinical picture and the good response to SRIs supports its clssification as an OCDSD.[13]

The differences in symptomatology between OCD & BDD is in the ideational content of the obsessional symptoms where the content in BDD reflects a sense of self as ugly and unlovable, while OCD symptoms involve fear of harm and danger. These feelings in BDD cause sense of shame and low self esteem very frequent. Both OCD and BDD symptoms can involve highly complex ideation content consistent with higher cortical functions. OCD symptoms can also include simpler behavior like tapping that may implicate striatal involvement .BDD is more likely to demonstrate over value ideas and delusional ideation.[23]

There are promising indication from case reports and exploratory studies that SR blocker such as Clomipramine, Fluoxetine and Fluvoxamine are superior to standard Neuroleptics and Benzodiazepines.[23,25]

Mood Disorders:

Depressed children frequently struggle with obsess ional ideas about committing suicide and ruminate a great deal about their self-worth and love. Mood disorders with depressive and/or manic episodes occur frequently in OCD patients and represent a therapeutic challenge. OCD patient treated with SSRT can develop a clinical syndrome characterized by insomnia, expansive or dysphoric mood, aggression, reckless acts، impulse dyscontrol and impaired insight. When a depressive syndrome appears in an OCD patient already on treatment, the therapeutic strategy become more complicated. The depressive symptoms may be just 2ry to OCD symptoms.[12]

Childhood Psychosis:

Clinical reports indicate that patients with psychotic OCD have more severe form of the illness and poorer treatment response than those with neurotic obsessive-compulsive patients. In addition, lower levels of functioning and worse long-term outcome in obsessive-compulsive schizophrenia compared with matched non-obsessive schizophrenia.

Bender (1955) described schizophrenia in childhood and mentioned that one of the forms is "Pseudoneurotic Syndrome" that occurs in early or mid childhood. It is marked by neurotic-like symptoms such as obsessions, anxiety, phobias, stereotype movements and compulsive activities with psychosomatic concern about body boundaries. She also described a term called "Pseudopsychopathic Syndrome" that is seen in children of 10 years of age or older who tend to act-out antisocially. They show paranoid ideation, compulsive aggression and potentially dangerous behavior with little evidence of insight.[43]

Epilepsy:

OCD symptoms may be present in specific forms of epilepsy. Forced thinking as a cognitive aura that may be experienced as a stereotypic out of context and irrational thoughts, is to be distinguished from OCD obsessions which is ego dystonic Obsessionality has been attributed to temporal lobe epilepsy such as that of automatic writing. There is no clear evidence that OCD is more prevalent in epileptics than in healthy individuals.[16]

Management

It appears that the heterogeneous pattern of co morbidity has implication for the pharmacological treatment of juvenile OCD and OCSDs youngsters. Neurochemical studies proved Serotonergic system to be specifically responsible for the wide range of phenotypic presentation of OCSDs. The compulsive and impulsive disorders have a differential response according lo the baseline function in neurochemical substrate. Novel pharmacological approaches such as multiple targeted pharmacotherapies for each set of symptoms have been tried.OCD and OCSDs display a preferential response to SRIs and behavioral therapy، nor epinephrine reuptake inhibitors on the other hand have not been effective. The OCSDs are less well characterized than OCD. Treatment for OCSDs has been determined predominantly by open clinical trial.[1]

Compulsive disorders such as OCD, BDD, hypochondriasis and anorexia nervosa may respond preferentially to SRIs. Because they stimulate the 5 HT activity, symptoms may initially worsen, following acute administration with high doses.Chronic treatment with these agents however may work to desensitize or down regulate 5 HT receptors over time[35]. The compulsive disorders have a long lag period before they respond to SRI، however after the initial response it can be maintained through giving an adequate trial with high enough dose. Impulsive disorders have a quicker response to SRIs, but their response can decrease over time with continued treatment. Therefore, treatment augmentation may be important once the patient is initially stabilized[13].

It is to be mentioned that behavioral disinhibition is relatively common and occasionally serious problem that appears in pediatric subjects and may preclude SSRIs initially without concomitant addition of mood stabilizer or atypical neuroleptics. It is

a dose related phenomenon and has a late onset (after 4 weeks). It appears that in addition to reduction of compulsive symptoms it may cause behavioral inhibition in a number of Domains that may in turn cause difficulties for the treated child[11]. For patients who partially respond to SSRI, augmentation strategies may be considered. Clonazipam is sometimes used or a neuroleptic if a tic or schiz-otypal personality disorder is co morbid.[19]

Dopaminergic mechanisms may also be involved in OCSDs, particularly those with simple motor symptoms, such as Tourette's syndrome or trichotillomania or those with psychotic features such as BDD or delusional OCD. Halloperidol and Pimozide have been effective in trichotillomania.[45]

The autoimmune disturbance PANDAS and its correlation with the development of some disorders in OCSDs through the antibodies reacting to neuronal tissue in basal ganglia generated greater interest both as; possible model for the development of neuropsychiatry symptom and for implication of antibiotics for streptococcal infection, can affect OCD and Tourettes's disorder severity. Measurement of anti streptolysin 0 titre (ASOT) or Anti-DNAs B-antibodies may be beneficial.[11]

Behavior modification should be considered in addition to medication. Patient treated with medication and cognitive behavioral therapy has greater improvement rate and lower relapse rate. Cognitive behavioral therapy as the first treatment of choice for all prepubertal children who present with primary OCD and for adolescents with mild or moderate OCD on children Yale-Brown obsessive compulsive scale. The efficacy of individual CG family therapy and group behavioral family therapy were found to be equally effective to reduce OCD symptoms for children and adolescent as individual treatment for children with the disorder. It has also shown considerable success with certain OCSDs. The technique of exposure and response prevention was first shown to be effective in the OCD patients. This technique involves graduated exposure to the feared stimulus with simultaneous prevention of anxiety reducing ritualistic behaviors. The patient thus becomes desensitized to the anxiety-provoking stimulus and no longer relies on compulsions to regulate anxiety[2].

Habit reversal, which involves identification of the behavioral antecedent and then substitution with a less problematic behavior has been reported to be effective in trichotillomania.[7]

Some success was found with BDD using systematic desensitization, exposure therapy and self-confrontation.[1]

Additional individual and family psychotherapeutic measures as well as pharmacological and educational intervention are often necessary. For some treatment-refractory patients, neurosurgery may be therapeutic.

Summary and Conclusion

Consistent research suggests some shared clinical features between the OCD and OCSDs including symptom profile, family history, neurobiological findings and treatment response. Co morbidity of psychiatric disorders in childhood and adolescence is the rule. Single diagnosis is the exception. They may call for more work in the Held of management. OCSDs in childhood are characterized by the inclusion of developmental disorders together with feeding and eating disorders, tic disorders,

impulse control disorder, somatoform childhood psychosis and organic disorder.

The greater focus on complex preservative pattern in early years of the disorder has lead to consideration of a broad group of behavior in relation to OCD. It is clear that everyday habit or isolated mannerism that is common in normal development seem quite distinct from OCD, as these have no predictive behavior within a community sample.

There are some other repetitive unwanted behavior of childhood onset that fall into the OCD spectrum crossing the current diagnostic categories such as; TTM and Onycophagia, that may actually be variants of OCD but are still not responsive to treatment profile unique to OCD

Feeding and eating disorders and Kleptomania have been suggested candidates for OCD spectrum with behavioral response to SRIs

Pharmacological response to SRI suggests the role of 5HT in the etiology of OCSDs. Still, some of the spectrum disorders have limited or no response and need augmentation therapy that suggests the involvement of other neurotransmitters in the pathogenesis of OCD.

Recommendations:

Theorizing that the episodic forms of OCD, Tourette's syndrome and Sydenham's chorea might be related to CNS autoimmune reaction (PANDAS), require more studies concerning the effect of immunosuppressive treatment as well as the effect of long-acting Penicillin

Available family, genetic and neurobiological findings concerning the wide range of all OCSDs are challenging. Family and genetic findings suggest that this spectrum might be different phenotypic presentation of an underlying gene or genes. Further research is needed for understanding of subtypting and more specific characterization of OCSDs.

Neurobiological findings suggest abnormalities in the subcortical and fronto-temporal cortical regions with disturbed neurocortical circuit connections in some of the spectrum disorders. Further research work is needed to elaborate its role in the genesis of different OCSDs.

More controlled studies on children and adolescents are needed to evaluate the effect of SRI and compare it with other medications for better understanding and management of OCSDs.

Less rigorous data are available for the effect of other psychotherapeutic modalities in OCSDs. Further studies are also needed to compare pharmacological versus other psychotheraputic measures in the management of OCSDs.

REFERENCES

1. Hollander E. and Rosen J. (2000): Obsessive compulsive spectrum disorders. A review. In Maji M., SartoriousN., Okasha A., ZoharJ. (eds). Obsessive compulsive disorder. WPA series. Evidence and experience in psychiatry. John Wiley & Sons LTD p. 203- 22
2. Brynsaka A, (1998): Obsessive compulsive disorder in children and adolescent; A literature review part II psychiatry, pol. Jan-Feb 32 (I): 27-88.
3. Cardona X., Avila A. (2000): Obsessive compulsive disorder and structural cerebral Alterations. Description of 3 cases. Neurologia Jun-Jul; 15 (6): 523-7.
4. Stein DJ. (2000): Advances in neurobiology of obsessive compulsive disorder. Implication for conceptualization putative obsessive compulsive and spectrum disorders. Psychiatric. Clin. North. Am J Sep. 23 (3) 545-62.
5. Diagnostic and Statistical Manual of Mental Disorder 4 Ed. (DSM-VI) (1994): American psychiatric Association. Washington D.C.

6. Castellanos X.F. (1998): Tic disorder and obsessive compulsive disorder. Child psychopharmacology. Btimothy Walsh E.D.Am Psych. Press. Washington D.c. London, England.
7. Cohen L.S., Simeon D.,Hollander E. and Stein J.D. (Obsessive compulsive disorders; Diagnosis, Etiology, Treatment Marcel Deker Inc. New York, Basel. Hong Kong
8. Hollander E., DelGiudic Asch G.y Simon L., Shemidler J. et al., (J999): B Lymphocyte antigen D8/17 and repetitive behaviors in autism Am. J. Psychiatry. 156; 317-320.
9. Flament F.M., Cohen D. (2000): Child and adolescent obsessive compulsive disorder. A review; In Maj M., Sartorious N., Okasha A., Zohar J., lst ed. 2000. John Wileys sons LTD.
10. Flament M. and Cohen D. (1999): Comorbidity and spectrum disorder in childhood onset obsessive compulsive Disorder Neuropharmacol. 9 (Supp! 5) 51 K6.
11. Geller D., Biederman J., Grffin S. et al (1996): Comorbidity of Juvenile obsessive compulsive disorder with disruptive behaviour disorder. J-Am. Acad. Child Adolesc. Psychiatry 35: 1637-1646.
12. Reddy V.C., Ready P.S., Srinulh S., Khanna S., Sheshard S.P., Girimai S.C. (2000): Comorbidity in Juvenile obsessive compulsive disorder ; A report from India. Can J. Psychiatry April; 45 (3) 274-8
13. Hollander E. and Benzaquen D.(1998) Psychobiology of compulsive spectrum disorders.In HollanderE and Stein D.(eds).Obsessive Compulsive Disorder Diagnosis,Etiology. Treatment. Marcel Deker. New York,Base<Hong Kong.
14. Okasha A, Ragheb K., Attia A.H. et al. (2001) : Prevelancc of obsessivecompulsive symptoms in a sample of Egyptian adolescents. L'Encephale, XXVII: 8-14.
15. March J, Frances A, Kah D et al (1997a) expert consensus guidelines: Treatment of obsessive – compulsive disorder. J clin psychiatry 58:1.
16. Dennis P., Cantwll S., Michael R. (1995): Classification conceptual Issues and Adolescent psychiatry; Modem approaches, RIackwell scien.
17. Paul Barrett , Larra Healthy-farrell and Johns March : congnitive - behavioral family treatment of childhood OCD : A controlled trial J. of American academy of child & Adolescent psychiatry 43:1 Jan 2004.
18. Bradley S'., Thomas P. (2000): Tourette's syndrome: what are we really imaging. In Ernst M., Rumsey M.J., Coyle T.J. (eds.). Functional neuroimaging in child psychiatry Textbook. Cambridge University Press- PP. 242-245
19. Leonard H.L., Leanne M.C., Swedo S.E., Rettew D.C., Gershon E.S., Rapoport J.L. (1992): Tic and Tourette's disorder. A 2-7 year follow up study of 54 obsessive compulsive children. Am. J. Psychiatry 149: 1244-1251.
20. Swedo S.E., Leonard H.L., Mittlentan BB et al., (1997): Identification of children with pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections by a marker associated with rheumatic fever- Am. J. Psychiatry- 154: 110- 11.
21. Cohen L.S., Simeon D., Hollander E. and Stein J.D. (2000): Obsessive compulsive spectrum disorder. In Hollander H., Stein D (eds.) Obsessive compulsive disorders; Diagnosis, Etiology, Treatment Marcel Deker Inc. New York, Basel. Hong Kong.
22. Henrry C.M., Perlmuller J.J., Swede E.S. (1999): Anorexia OCD and streptococcus. J. Am. Acad. Child. Adolesc. Psychiatry. 38: 3 March.
23. Eddy M.F. Walbroehl G.S. (1998): Recognition and Treatment of obsessive compulsive disorder. Am. Fam Physician Apr 1; 57(7) 1623-8.
24. Kaye W.H., Greene C.G., Moss H., et al. (J998): Alteration in Seretonine activity and psychiatric symptoms after recovery of Bulimia nervosa.Arch.Gcn.Psychiatry. 55:927-93
25. Ernst M, Zametw J.A., Jons H.P. et al (1999): High presynaptic dopaminergic activity in children with Tourette's Disorder. J. Am. Acad. Child. Adolesc. Psychiatry January 38(1), 86-93.
26. Ernst M., Zametzin A.J., Matochik J.A Johns P.II., Cohen R.M. (1998): Presynaptic dopaininergic activity in ADI ID adults; a (l'luorine-18) Flurodopapositeron emission tomography study. 1. Neuro Sc: 18:5901-5907.

27. Moore G.J., Mac Master P.P., Stewart C and Rosenberg D.R. (1998): Caudate glutamatergic changes in paroxietine therapy to pediatric obsessive-compulsive disorder. J. Am. Acad. Child. Adolesc. Psychiatry. 27,663-7.
28. Rosenberg D.R., Mc Master F.P., Parrish J.K. et al., (1998): 1-HMRS measurement of caudate glutaminergic changes associated with paroxetine therapy for pediatric OCD. Ernst M., Rumsus M.J. and Coyle T.J (eds.). Functional neuroimaging in child Psychiatry Cambridge. 224-228
29. Giedd, J. Vaituzis A.C., Hamburger S.D. et al, (1996): Quantitative MRI of the temporal lobe amygdala and hippocampus in normal human development; Ages 4-18.J- Compar. Neuro, 366, 223-30
30. Chowdhury U., Gordon. L., Lask B, (2000): Eating disorders in Ernst M., Rumyey MJ. And Coylc J. (ed.s.) Functional neuroimaging in Child Psychiatry. Cambridge University Press
31. Peterson &&, Riddle M.A, Cohen D.J., et ul., (1993): Reduced basal ganglia volume in Tourette's syndrome using three dimensional reconstruction techniques from magnetic resonance images. Neurology, 43: 941-949.
32. Castle D.J., Groves A (2000): The internal and external boundaries of obsessive compulsive disorder. Aust NZ J. Psychiatry. April ; 34 (2); 249-55.
33. Pronko N.H. (I966): Obsession- Compulsion. Textbook of abnormal psychology. Williams & Wilkins. Baltimore. Pp. 213-230
34. Nemiach l.C., (1967): Psychoneurotic disorder II. Obsessive-compulsive and neurotic depressive reaction. In "Freeman A.M., Kaplan H.I., (ed.)". Comprehensive textbook of psychiatry. Williams & Wilkins. Baltimore.
35. Zohar A.H., Ratzosin G., Pauls D.L., el.al., (J992): An epidemiological study of obsessive compulsive disorder and related disorders in Israeli. Adolescents. J. Am. Acad. Child. Adolese. Psychiatry. 31:1057-1061.
36. Berganza C-f., Cazall L, Gailan, Mezzich J, (1996): Criterion validity of child health scale. Revista Latinoamerican de Psicologia. 28, 317, 339.
37. Valleni -Basile L.A., Garrison CZ, Waller A, et al, (1996): Incidence of OCD in a community sample of young adolescents. J. Am. Acad. Child-Adolesc,; 35(7)898- 906
38. Apter A, FaLLon T.L., King R.A., Ratzon, G.Zohar A.H. et al (1996): Obsessive-compulsive characteristics. From symptom to syndrome J. Am Acad. Child Adolesc.Psychiatry. 35:906: 917
39. El-Rakhaway M. (1992): An Egyptian study concerning obsessive manifestations & symptoms in children. Master thesis in psychology .Ein-ShamsInstitute of post graduate childhood studies. Department of psychological studies.
40. Hollander E. (1998): Treatment of obsessive compulsive spectrum disorder with SSRI. Br. J. Psychiatry Suppl. 35: 7-12.
41. Morialy J., Compos Costa D., Schmitz B., Trimble M.R., Elt P.J. and Robertson M.M. (1995): Brain perfusion abnormalities in Gilles de la Tourret's syndrome. Br. J. Psychiatry 167, 249-54.
42. Rose E.A., Porcerelli J.H, Neal A. K (2000): Pica: Common but commonly missed J. Am. Board Fam. Pract. Sept.-Oct; 13 (5): 353-8.
43. Abdel-Rahman S. (1987): Childhood Neurosis in "Essentials in Child Psychiatry" Pp. 189-198
44. Schmidt U., Hodes M, and Treason J. (1992): Early onset anorexia nervosa who is at risk? Psycho! Med. 22, 623-K-
45. Stein D.J. Hollander E., Cohen L., Simeon A, Aronowitz R. (1995): Serotonergic resposivity in trichotillomania neuroendocrine effects of m.chlorophenyl-perazin. Biolog. Psychiatry 37: 414-416.
46. Lepkifker E., Darmon P.N., Ziv R., Lancu I., Horesh N., Koller M. (1999): The treatment of kleptomania with serotonin reuptake Inhibitors. Clinical Neuropharmacol Jan-Feb, 22 (1) 40-3.