Obsessive Compulsion Personality Disorder (OCPD) and Obsessive Compulsion Disorder (OCD) associated with Digital Arches, Constipation/Colonic Inertia and Dysautonomia; Genetically Linked Traits, linked with "The Pathology of Control and Stopping." A Review.

OCPD with Digital Arches, Constipation & Dysautonomia; (*running title*)

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Abstract;

The Dermatoglyphic (Fingerprint) evidence for a congenital syndrome of constipation is reviewed and the association of this in women with Obsessive Compulsive Personality Disorder (OCPD) and Obsessive Compulsion Disorder (OCD) is presented. Colonic inertia in young severely constipated women may occur and the pathophysiology of colonic inertia and chronic constipation along with association with Obsessive Compulsion Personality Disorder or OCD. Significant dysautonomia is seen in these disorders. Myenteric plexus abnormalities and verification of colonic inertia with long redundant colons often predisposing to incomplete colonoscopies supplemented with CT Colonoscopy (CTC) is discussed. A review of Literature is made concerning OCPD and OCD constipation, genes and pathophysiology. "The Brain's Inability to See That Something is Safe," causes OCPD. The "Pathology of Stopping not Starting "occurs in OCD. DNA methylation and dysfunction in serotonergic signaling occurs in OCD.

Heart rate variability in IBS and constipation is abnormal. Therapy with Exposure Response Prevention (ERP) therapy, SSRI, QEEG, and Neurofeedback along with (PBM) photobiomodulation is discussed.

Key Words;

Digital arches, Obsessive Compulsion Personality Disorder (OCPD), Obsessive Compulsion Disorder (OCD), constipation, colonic inertia, dysautonomia, DNA methylation.

BACKGROUND:

Sheldon Gottlieb and Marvin Schuster at Johns Hopkins published their landmark paper "Dermatoglyphic (Fingerprint) Evidence for a Congenital Syndrome of Early Onset Constipation and Abdominal Pain," in 1985 which reported a marked increase in the prevalence of the dermatoglyphic pattern of digital arches in patients with early onset (before age 10 yrs.) idiopathic constipation and abdominal pain. See figure 1 below for image of Digital Arches.

1. Finger Print Patterns, Loops, Whorls, and Arches

They described the clinical features associated with digital arches among 155 consecutive patients referred for gastrointestinal consultation. They compared the clinical features of the 31 patients with one or more digital arches with 31 controls without arches chosen by computer matching from the overall group. They suggested a congenital etiology for early onset idiopathic constipation and abdominal pain by their strong association with the dermatoglyphic pattern of digital arches. They observed sixty-four percent of patients with constipation and abdominal pain before age 10 years had one or more digital arches had one or more digital arches, compared with 10% of patients without constipation and abdominal pain [$p < 0.001$). Seventy percent of constipated patients with arches had the onset of symptoms before age 10 years compared with 23% of constipated patients without arches [$p < 0.001$) and 14% of patients with symptoms other than constipation [$p < 0.001$). They concluded that this dermatoglyphic pattern has an autosomal dominant mode of inheritance with nearly complete penetrance. They found the association between chronic intestinal pseudoobstruction and digital arches was especially noteworthy. All of these patients were women and most of them (59%) had the onset of constipation and abdominal pain in childhood. It was among these patients that the highest prevalence (65%) of digital arches was seen. [1]

TJ Pulliam and MM Schuster published "Congenital makers for chronic intestinal pseudoobstruction" in 1995. They examined fingerprints in 1566 consecutive gastrointestinal specialty referrals. In 43 patients, the initial diagnosis of CIP was confirmed by subsequent testing. Since the digital arch is the least common (10%) of the three patterns of fingerprints (arches, loops, and whorls) found in primates, they also found that the presence of digital arches (DA), mitral valve prolapse (MVP), joint laxity (JL) and previous history of constipation before age ($C<10$) proved significantly higher ($p < 0.001$) in CIP patients than in age- and sex-matched controls and the general population. They reasoned that CIP may be a heritable syndrome because it is associated with heritable congenital markers (DA, MVP, JL, and $C < 10$. Furthermore since these markers are identified with higher frequency in CIP patients than in the general population and in age- and sex-matched patients with other gastrointestinal disorders, all four markers are easily detectable, and their recognition could lead to earlier diagnosis of the disorder.[2]

However, Gottlieb and Schuster were never aware of the connection of digital arches in women with obsessive compulsive disorder. This review will detail why this phenotypic expression of digital arches is associated with the syndrome of OCD, OCPD, constipation and *autonomic imbalance.*

Complaints of constipation in obsessive-compulsive disorder in a randomized controlled trial was reported by CS North and associated in 1995. Data from the Epidemiologic Catchment Area project collected with the Diagnostic Interview Schedule were analyzed to determine the association, if any, of complaint of medically unexplained constipation with a diagnosis of obsessive compulsive disorder (OCD). They found history of constipation was significantly associated with a lifetime diagnosis of OCD in women (not men), even when controlling for symptom-reporting biases using number of other positive somatoform symptoms. Other psychiatric disorders were commonly implicated with functional bowel complaints- such as major depression and panic disorder. They concluded that the lack of association of constipation with OCD in men in a general population sample failed to support psychoanalytic concepts that historically have linked these two phenomena. [3]

Masand and associates at Duke in 2006 provided more evidence by determining the prevalence and phenomenology of IBS in patients diagnosed with obsessive-compulsive disorder (OCD). A semi-structured diagnostic interview was administered to patients seeking treatment for OCD in outpatient settings. Structured questions regarding gastrointestinal functioning and IBS symptoms were administered and IBS was diagnosed by a gastroenterologist using Rome I criteria. Thirty-five percent with OCD met criteria for IBS. Of these, 53.8% had IBS with both diarrhea and constipation, 30.8% had diarrhea-predominant IBS, and 15.4% had constipation-predominant IBS. [4]

As for constipation, in 1994, ninety patients suffering from obsessive-compulsive disorder (OCD) diagnosed according to International Classification of Diseases (10th edition [ICD-10]) criteria attending the outpatient clinic of the Institute of Psychiatry in Cairo in 1991-1992 were assessed by the Yale-Brown Obsessive-Compulsive Scale (Y-BOCS) for symptomatology and

severity of symptoms. Twenty percent of patients had a positive family history for OCD. The most commonly occurring obsessions were religious and contamination obsessions (60%) and somatic obsessions (49%), and the most commonly occurring compulsions were repeating rituals (68%), cleaning and washing compulsions (63%), and checking compulsions (58%). [5]

Furthermore constipation in 8 patients was found in a group with 40 OCPD in a study of 100 patients with Parkinson's disease without relation to dopanergic medication. [6]

Colonic inertia in young severely constipated women;

Colonic Inertia was first used to describe a syndrome of colon slow emptying and anorectal motility in young women in 1986. A series of 64 women complaining of severe constipation was described, in each of whom delayed elimination of markers from the colon was demonstrated but a barium enema was normal. Comparison with the control group showed no evidence that the patients had been underweight at any time and treatment with a bran supplement did not usually help them. These patients experienced rectal sensation before defecation less often than the control subjects and they used digital pressure to assist defecation more frequently. These women with constipation tended to have more painful and irregular menstrual periods. Hesitancy in starting to pass urine was more common, as were symptoms such as cold hands or blackouts suggesting *dysautonomia.* [7]

Another report of women with severe idiopathic constipation in 1988 was conducted by Waldon et al in Alberta Canada. They assessed forty-four severely constipated women and a control group (8 female, 8 male) asymptomatic volunteers who underwent assessment of colon function by clinical examination, rectosigmoid intraluminal pressure recording, colonic transit utilizing radiopaque markers, anorectal manometry, and rectosigmoid electrical activity. They concluded that a neural abnormality affecting afferent nerves may be present in the rectum of female patients with severe idiopathic constipation. [8]

Another group analyzed clinical, radiographic, esophageal manometric and pathologic features of 26 women with severe, idiopathic constipation. On barium enema examination, 9 of 24 patients had colons of increased length and 4 of these 9 patients had colons of increased width

(greater than 10 cm. Twelve patients underwent subtotal colectomies for constipation. Silver stains of the myenteric plexus showed quantitatively reduced numbers of argyrophilic neurons in 10 patients. Pathology demonstrated morphologically abnormal argyrophilic neurons, decreased numbers of axons and increased number of variably sized nuclei within ganglia in all. They concluded severe idiopathic constipation is associated with a pathological abnormality of the myenteric plexus. [9] Numerous motility disorders are associated with the colon: constipation, irritable bowel constipation predominant along with intussusception, and others. . Defects in nitrergic nerves are believed to underlie several serious motility disorders including the myenteric plexus of familial *dysautonomia* patients. [10].

Verification of Chronic Constipation with long redundant colons with CT Colonoscopy (CTC);

CTC was first introduced in 2008. CT colongraphy interpretation courses were sponsored by the American Gastroenterology Association thereafter. Dr. David Kim who along with Dr. Perry Prickhardt at the University of Wisconsin, both of whom have the most experience with CTC told the audience "why there were so many female redundant colons in the teaching CTC test file." Kim said, "Whom do you think where referred for CTC due to incomplete colonoscopy? [11]

In "Approach to Incomplete Colonoscopy: New Techniques and Technologies" by Franco and Associates listed incomplete colonoscopies due to inadequate bowel preparation, discomfort and intolerance, low body mass, female sex, and young age. CTC is often performed after incomplete colonoscopy. A prospective study evaluating 10,571 colonoscopies found 546 patients with incomplete colonoscopy due to redundancy and tortuosity underwent CTC in their study. [12]

A review of Literature concerning OCD, Constipation, Genes and Pathophysiology:

Quality of Life (QOL) in Women with Constipation in Australia was conducted on the impact of persistent constipation on health-related quality of life and mortality in older community-dwelling women. Of the 5,107 women surveyed, 24.7% reported having persistent constipation on at least 4 out of 5 surveys, and transient constipation reported on 1-3 surveys. Women

reported persistent constipation had significantly lower scores for all sectors of QOL, and had higher levels of self-reported depression. Mortality rates were increased when comparing women with no reported constipation with persistently reported constipation (8.2% vs. 11%, odds ratio = 1.32, 95%. The authors reflected on the higher mortality rate that it seemed more likely, that constipation was a marker of more serious underlying disease (such as cancer) or reflects the use of constipating medications (such as cardiac medications associated with poorer cardiovascular outcomes) and depression. [13]

PATHOPHYSIOLOGY:

According to Hinds et al. in obsessive-compulsive disorder (OCD), individuals feel compelled to repeatedly perform security-related behaviors, even though these behaviors seem excessive and unwarranted to them. They reasoned (1) a dysfunction of activation—a starting problem—in which the level of excitation in response to stimuli suggesting potential danger is abnormally strong; versus (2) a dysfunction of termination—a stopping problem—in which the satiety-like process for shutting down security-related thoughts and actions is abnormally weak. The intensity of activation of security motivation was measured objectively by change in respiratory sinus arrhythmia using heart rate variability. Results: OCD patients with washing compulsions were significantly less able to reduce this activation by engaging in the corrective behavior of hand-washing. The results of these experiments demonstrated that OCD reflects impairment in the ability of security-related behavior to terminate motivation evoked by potential danger, rather than a heightened initial sensitivity to potential threat. OCD is due to a dysfunction of stopping. They concluded then the dysfunction of neural pathways is in the brain stem that fails to turn off this activity. [14]

Significant Dysautonomia in OCD, OCDP and other Psychiatric Disorders

The finding of significant dysautonomia was observed in patients with Joint Hypermobility, in phobic , obsessive compulsive disorder and OCPD by JA Eccles in 2015 [15] This was verified again in 2016 by GA Alvares who fond anxiety-related disorders- panic, generalized anxiety, social anxiety, PTSD or obsessive –compulsive disorder, and social phobia with *autonomic nervous system dysfunction.* [16]

Another finding was the usual body habitus of such females is being slender. Constipation is often associated with slow gastric emptying. [17] The often association in these patients with OCD has been described, but the following mechanism is just now being described.

The Brain's Inability to See That Something is Safe, Causes OCD;

According to a new report in New Scientist by Claire Wilson, the repeated thoughts and urges of obsessive compulsive disorder (OCD) may be caused by an inability to learn to distinguish between safe and risky situations. They used Focused therapy for OCD that is known as Exposure Response Prevention (ERP) therapy which involves patients trying to experience their triggers without doing their accompanying rituals – such as touching a toilet seat without washing their hands afterwards – to learn that nothing bad happens. Fineberg stated new findings may explain why people with OCD find this approach so difficult and it can take so long. "The bit of their brain that should be telling them it's safe isn't working. Now we can say to them this is why it's taking so long and we should stick with it." [18}

Brain genetics in OCD;

OCD is a severe psychiatric disorder also linked to abnormalities in glutamate signaling and the cortico-striatal circuit. Precisely the psychiatric states may result from an imbalance of excitatory glutamate and inhibitory GABAergic neuron differentiation, a process that involves the genes NRXN1 a synaptic cell-adhesion protein, REEP3 with possible role in synaptic plasticity, calcium signaling, CTTNDP2 a G-protein-coupled serotonin receptor as well as PTPRD, a protein tyrosine phosphatase (PTP) family. PTPs are known to be signaling molecule. The team at the Broad Institute sequenced coding and regulatory elements for 608 genes potentially involved in obsessive-compulsive disorder in human, dog, and mouse. Using a new method that prioritizes likely functional variants, they found four strongly associated genes, validated in a larger cohort. Their findings suggest synaptic adhesion as a key component in compulsive behaviors. [19]

Dopamine receptor gene variant DRD3 in OCPD

Preliminary evidence for an association between dopamine receptor gene variant DRD3 and OCPD with major depression was published in 2006 by Light et al. [20] This dopanergic variant may well explain their obsessive compulsion for “safety and cleanliness” which Sigmund Freud once labeled as “anal- retentive” in his “Theory of Psychosexual Stages.”[21]

DNA Methylation in OCD;

DNA methylation may regulate expression of genes as the heritable epigenetic modification. Examination for genome-wide DNA methylation was performed on blood from patients with OCD, as well as healthy control subjects. 8,417 probes corresponding to 2,190 unique genes were found to be differentially methylated between OCD and healthy control subjects. Of those genes, 4,013 loci were located in CpG islands and 2,478 were in promoter regions. These included BCYRN1, BCOR, FGF13, HLA-DRB1, ARX, which have previously been reported to be associated with OCD. Since the literature have suggested that not only genetic but also environmental factors accounted for susceptibility of obsessive-compulsive disorder, these results therefore strongly suggested that “differential DNA methylation” might play an important role in etiology of OCD. [22]

Defects in DNA Methylation may have ties to diseases in which dysautonomia is significant. For example dysautonomia is associated with Ehler-Danlos Syndrome (EDS) and mast cell diseases, as well as a number of other disorders of hypermobility. Thus folate deficiency and Methylenetetrahydrofolate Reductase (MTHFR) gene defects hinders DNA synthesis and cell division as well as DNA methylation. *Dysautonomia* is associated with EDS as well as mitral valve prolapse. [23]

Dysfunction of Serotonin Signaling;

Hypomethylation of gene is another problem. For example, dysfunction of serotonin signaling and HTR2A receptor are involved in the pathogenesis of schizophrenia (SCZ) and bipolar disorder. Mutations in this gene are associated with susceptibility to schizophrenia and obsessive-compulsive disorder, and are also associated with response to the antidepressant citalopram in patients with major depressive disorder. [24]

Serotonin function in obsessive-compulsive disorder has been studied since the 80's. Serotonin has thought to play a role in the pathophysiology of obsessive-compulsive disorder (OCD) because of the anti-obsessional effect of selective serotonin reuptake inhibitors (SSRIs). [25]

Baumgarten and Grozdanovic in another study of the medical literature reviewed the role of serotonergic neurons in brain function, studies on monoamine metabolites in cerebrospinal fluid (CSF), various stress neuropeptides, neuroendocrine and behavioral challenge after administration of direct and indirect serotomimetic compounds, and neuroanatomical data on brain circuits organizing behavior. The authors concluded that continuous treatment with SSRIs alters serotonin turnover and neuropeptide expression patterns in OCD-entertaining functional forebrain/midbrain circuits. Low serotonin levels have been observed in Positional Orthostatic Tachycardia (POTS) and patients with *dysautonomia.* [26]

Mucosal serotonin signaling is also altered in chronic constipation but not in opioid- induced constipation. [27}

QEEG Neurofeedback in OCD

A study in 2011 by Tanju Siirmeli and Ayben Ertem of 36 drug resistant subjects with OCD were assigned to 9-84 sessions of QEEG-guided Neurofeedback (NF) treatment. Daily sessions lasted 60 minutes where 2 sessions with half-hour applications with a 30 minute rest given between sessions were conducted per day. Thirty-three out of 36 subjects who received NF training showed clinical improvement according to the Yale-Brown obsessive-compulsive scale (Y-BOCS). The Minnesota multiphasic inventory (MMPI) was administered before and after treatment to 17 of the subjects. The MMPI results showed significant improvements not only in OCD measures, but all of the MMP1 scores showed a general decrease. They concluded by physician evaluation of the subjects using the clinical global impression scale (CGI), that 33 of the 36 subjects were rated as improved. [28]

QEEG- Guided Neurofeedback therapy efficacy was tested in decreasing OCD symptoms. The results using the Kuruskal– Wallis and Mann-Whitney U test were analyzed. They concluded that neurofeedback treatment may be used as a new treatment approach for treating OCD. [29]

Marvin Berman PhD at Quietmind Foundation who has pioneered the use of QEEG Neurofeedback with NIR LED Light Helmet therapy has experienced success in therapy in OCD and OCPD subjects! [30]

PURPOSE:

The Relation between OCPD and OCD;

The cause of OCPD is thought to involve a combination of genetic and environmental factors. {30]. A few (but not all) studies have found high comorbidity rates between the two disorders and both may share outside similarities – rigid and ritual-like behaviors, for example. Behavior such as hoarding, orderliness, and a need for symmetry and organization for example, are often seen in people with either disorder. Viewpoints toward these behaviors differ between people affected with either of the disorders. Often OCD patients show an obsessive need for cleanliness, usually combined with an obsessive preoccupation for tidiness. Some OCPD individuals do have OCD, and the two are sometimes found in the same family according to Samuel's research [32] and occasionally along with eating disorders. In general, patients with OCPD do not generally feel the need to repeatedly perform ritualistic actions, common symptom of OCD, and usually find pleasure in perfecting a task, whereas people with OCD are often more distressed after their actions. [33] Berg et al contended that the direction of the relationship is obscure, and it might be that OCPD develops as a coping strategy after the onset of OCD. [34]

Post Prandial Autonomic Nervous Activity in IBS, Constipation Predominant:

In a recent study published by Whitehead and Drossman and Japanese colleagues, Y.Tanaka et al. in Journal of Neurogastroenterology and Motility using heart rate variability (HRV) cited that IBS patients showed a significant blunting sympathetic response to colonic distention. They didn't report any subtype of IBS (diarrhea predominant, mixed or constipation) that was more prone to this. [35] However, *dysautonomia* has been known to be prevalent in neurological diseases especially constipation in Parkinson's, post stroke, MS, spinal cord disease. [36]

It is not inconceivable that psychiatric disorders of OCD and OCPD have dysautonomia involved especially in those with constipation. For example, severe *dysautonomia i*n a primate model of OCD was observed after drug (biculline) injections of the ventricle anterior and medial dorsal nuclei of the thalamus with compulsive like behavior. Deep brain stimulation of the caudate or subthalamic nuclei ablated these actions testing the hypotheses of the role of the thalamus in the genesis of repetitive behaviors and related genesis. [37] Anxiety disorders are characterized by lower HF and lower high frequency power is correlated with stress, panic or worry. [38] A study by Cain KC et al demonstrated women with constipation predominant IBS and severe pain had lower HRV as high-frequency power. [39] This high frequency component of HRV reflects cardiac parasympathetic modulation rather than parasympathetic 'tone'. [40]

Havnen and associates in Bergan Norway found sleep disturbance characterized as late sleep onset in a significant number of OCD patients with reduced HF HRV! The authors concluded that the study was to their knowledge the first to indicate a relationship between cognitive inhibition and HF HRV in a sample of OCD patients. They stated that metaphorically speaking, primary insomnia might be the consequence of a stuck gas pedal (arousal) but rather a result of impaired brakes (inhibition). They cited that the relationship between HRV and cognitive inhibition supported the anticipated relationship between the role of executive functioning in the prefrontal cortex and *vagally mediated HRV*, indicating that relationship is also meaningful in OCD. [41]

Women, Constipation and Colonic Transit Time:

A Korean Study of Colonic Transit Time (CTT) in 42 health subjects found that women had a mean CTT that was longer than males (30:±21.4h versus 22.3±12.1h) but was not significant until they looked at luteal phase which was significantly longer than follicular phase. [42]

Conclusions; and Gedenkschrift to Marvin M. Schuster MD:

This manuscript for Journal of Neurogastroenterology and Motility is being written as a commemorative publication following the death of Marvin M Schuster MD, internationally known gastroenterologist at Johns Hopkins who passed May 12, 2017. Marvin was a friend and

colleague of many of us younger gastroenterologist as one of the pioneers in the field of Neurogastroenterology and Motility. He had received his BA in psychology, BS and MD degrees from the University of Chicago and did his subsequent training and spent his entire academic life at Johns Hopkins. He was the first to integrate full-time psychologist and medical faculty. He established the Johns Hopkins Amos Center for Mind, Body and Food. He discovered the digital arches in his patients with constipation at his motility center after being told of the correlation by Sheldon Gottlieb, a cardiologist. He referenced MH Swartz's publication of the dermatoglyphic studies of patients, 19 % of 100 whom had mitral valve prolapse and a control group of 100 with only 2.5% of all digits. [43] Marvin Schuster went on to have on his web site for his Motility Center at Johns Hopkins, "Clues at Your Fingertips." The gastroenterologists in this Baltimore Medical Center thereafter referred to this finding as "Schuster's Syndrome!"

Constipation occurs in 63 million Americans and many are not relieves by a high fiber diet, fresh fruits and vegetables and even over the counter suppositories and enemas. Medications such as Prucalopride as a prokinetic may finally help those patients with colonic inertia when other measures have failed.

The occurrence of constipation or colonic inertia in OCD and OCPD is more than happenstance, with genetic, significant *dysautonomia* and pathophysiological mechanisms affecting the brain gut axis with the phenotypic expression of digital arches! Accordingly, increased sympathetic activation with disturbed parasympathetic function was even found in constipation predominant irritable bowel. The authors concluded that central sympathetic influence within the brain gut axis is most probably responsible for the myoelectrical activity disturbance in IBS especially constipation predominant. [44]

The connection of constipation with OCD, OCDP and digital arches has implications of a low tech physical diagnostic method which could if widely disseminated, to early recognition and treatment of this "unspoken epidemic "of those who often suffer in silence!

Acknowledgements: No financial aid was received by the author in preparation of this manuscript and no Conflict of Interest! The author would like to thank Douglas Drossman MD, for suggestions and help in reviewing this manuscript.

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