Inflammation and grey matter alteration: Causes and effects in PTSD and OCD

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ABSTRACT

Diagnosis and treatment of obsessive and fear driven behaviours have gone through significant changes since the days medical bodies first started to take notice of them. Research in the past decades in the fields of psychology, psychiatry, neurology and biology has aimed at understanding underlying psychological and physiological conditions, triggers and circumstances that aid the development and sustenance of disorders that manifest in fear, anxiety, obsessive and in more severe cases, aggressive behaviour towards oneself and others. A literature review was conducted on neurological and grey matter alterations in patients with obsessive-compulsive disorder (OCD) and post-traumatic stress disorder (PTSD), with the aim of identifying evidence of OCD and PTSD comorbidity, physiological, neurological and biochemical changes in the brain, specifically grey matter reduction (GMR) and chronic inflammation, both of which may act as potential causes and consequences of the aforementioned diseases, as well as prevalence of genetic predisposition to fear, anxiety and stress related disorders. Research results showed that in order to evaluate, understand and diagnose mental health disorders, science, psychology and therapy must approach the topic of mental health through holistic lenses, factoring in genetics, biochemistry of the brain and the human organism as a whole and environment, with an appreciation of the individual case of each subject shaping their particular set of causality, symptoms and manifestation of the condition.

Keywords: *PTSD, OCD, pro-inflammation, immune system, anxiety disorders, grey matter reduction, comorbidities, genetics, twins.*

INTRODUCTION

The brain, as the main organ of the nervous system

The human brain, much like the two disorders this paper examines, has gone through a significant evolution in terms of our understanding of its role, function, structure and anatomy. Aristotle believed the brain to play the simple task of a cooling mechanism for the body. Since then, we know the brain to be the seat of higher cognitive functions and the main organ of the nervous system.

It is thanks to the brain that we are able to form memories, process thought and speech, make decisions that allow us to function normally in society, recognize danger and act upon that danger in a calculated manner. As such, the brain is a complex mechanism of interplay between over 80 billion neurons organized in areas and structures that support and complement each other so that a human being is able to process internal and external stimuli, apply healthy cognition and behaviour and lead a normal life. Consequently, injury or damage to the brain leads to degeneration of brain cells and affects the daily life of survivors and their families (Stocchetti and Zanier, 2016)

While a traumatic brain injury (TBI) offers doctors the chance of immediate evaluation of the damage, brain degeneration caused by tumours, diseases, mental and emotional trauma may go on undetected or unattended for years.

A brief review of OCD

The 14th to 16th century Europe. It was only in 1877 that German born neurologist and psychiatrist Carl Westphal upon observing extreme anxiety and obsessive thoughts in several of his patients, defined OCD as an independent psychiatric disorder (Oberbeck and Steinberg, (2015), influencing the later works of the likes of Pierre Janet and Sigmund Freud.

Thomsen's study (1999) offers a translation of Westphal's original text (1878) about the nature of compulsive behaviour as follows:

By compulsive ideas I mean ideas which, in an otherwise intelligent person and without being caused by a depressive or otherwise emotional imbalance, come to the forefront of his consciousness against his will. They cannot be dispelled and they impede and frustrate the normal chains of thought, even though the victim always considers them to be abnormal and strange. Most of the time they are absurd and have no provable connection to former ideas. To the patient they appear to be incomprehensible and appear out of thin air (p. 13).

Thomsen further argues that OCD is less likely a psychiatric condition and more a result of biological predisposition aggravated by external circumstances.

As we stand today, there is no consensus amongst scientists and researchers on the exact psychological, physiological and environmental mechanisms that determine the development of OCD. The multitude of theories around potential causes list genetic, neurobiological causes, pregnancy, learned behaviours, environmental factors, which may all trigger OCD alone or combined. Specific events may also lead to the development of the condition; however, it is not clear whether such an event acts as a cause or an activator of an already existing predisposition.

Clinical cases supporting both accounts have been recorded. Furthermore, in a critical literature review of the relationship between malnutrition and depression, Mattar *et al.* (2011) observes that OCD, as well as other depressive or anxiety disorders, are often a consequence of Anorexia Nervosa, an eating disorder characterised by compulsive self-starvation.

A brief review of PTSD

Conversely, it was only in 1952 that the Diagnostic and Statistical Manual of Mental Disorders (DSM-I) references a diagnosis of a condition labelled at the time as gross stress disorder, which today we know as post-traumatic stress disorder (PTSD). PTSD up until 2013 was labelled as an anxiety disorder. Symptoms have been clustered into main categories: intrusive negative thoughts, repetitive behaviour, avoidance of triggers that may make the person re-experience the trauma and arousal, which reflects in self destructive or aggressive behaviour towards others. In 2013, DSM-V reclassified PTSD under Trauma and Stressor Related Disorders (Regier, Kuhl and Kupfer, 2013). on the premise that though anxiety is an underlying symptom, the condition itself is a result of some trauma the patient has not been able to process.

Co-occurrence of OCD and PTSD

Though we notice an immediate distinction between the causes of OCD where multiple factors may contribute to the development of the disorder and PTSD being directly correlated with an unprocessed trauma (McFarlane, 2010a), the way these conditions manifest present a great deal of similarities, overlap of symptoms and an interconnectedness where OCD may present itself as a sequel of PTSD (Dykshoorn, 2014).

Over the years, the diagnosis of these conditions has been shaped by psychology, psychiatry and behavioural science and only in more recent decades findings from biology and neuroscience have started to shed light on the physiological and neurological alterations in the brain, grey matter reduction, changes in the immune system of patients with PTSD and OCD as well as the presence of chronic inflammation, which may act both as a trigger and as a condition that promotes the sustenance of these disorders.

The challenge for researchers, medical bodies and scientists lies in the diversity of research results, evidence often overlapping, non-conclusive or contradictory.

PTSD and OCD often co-occur and when they do, the severity of OCD symptoms has been observed to be proportionate to the severity of the suffered trauma, or the number of traumatic events in the patient's life. Medical bodies are also faced with the need to differentiate them, to identify the right sequence of treatment, be it psychological or prescription of drugs and further down the line they are challenged with the increasing need to identify measures that help with the detection of biochemical and genetic predisposition in order to successfully increase prevention rates.

Symptomatology of OCD and PTSD

OCD and PTSD have not only been observed to co-occur, but they also share a great number of symptoms and conditions that set them off. This review has investigated the overlap of symptoms as well as the differences that allow scientists and

therapists to identify cases where a patient may be suffering from both conditions concurrently or only one or the other with accompanying symptoms from other fear and anxiety-based diseases.

The onset of OCD may be triggered by an apparently insignificant event (the subject forgot the light on when they left the house), a traumatic event that first led to PTSD, followed by OCD, developed as a coping mechanism, or might start without any identifiable cause. The person is usually fully aware that the compulsive, socially or morally undesirable thoughts and behaviours make no sense, however he/she feels unable to stop them. According to Gavin's study (2018), OCD subjects seem to be "stuck in a Loop of 'Wrongness'".

Patients with PTSD may also experience obsessive thoughts; however, these thoughts are directly connected to one or multiple traumatic live events, by on one hand repeatedly reliving the details of those events and on the other hand compulsively avoiding stimuli that could trigger the emotional and mental pain caused by the event. In both cases, a neurocircuitry conditioning is gradually established in the brain that leads to what is commonly known as "what fires together, wires together" (Keysers and Gazzola, 2014).

The Pavlovian fear conditioning (Shin and Liberzon, 2010a) is important to be mentioned here. In both PTSD and OCD cases the patient is fearful of losing control of themselves or the situation. Though the obsessive compulsions are of different nature, both identify and connect previously learned neutral stimuli (a song, a sound, a name, a smell, a situation, etc.) to the anxious need to perform a ritual or relive the details of a painful trauma.

Research studies on GMR and inflammation in the OCD and PTSD brain

In a paper published in 2015 by Cheng *et al*., a team of researchers have shared their findings from a study involving voxel-based morphometry (VBM) and magnetic resonance (MR) imaging in order to compare grey matter volume (GMV) between PTSD, OCD and social anxiety disorder (SAD) patients. Selected participants were free of known neurological diseases, mental retardation or other medical or mental conditions that would have influenced the outcome of the results and have been recruited from checklists that qualified them as suffering from PTSD, OCD or SAD. Patients from these 3 groups were tested against healthy controls and the MRI results showed differences across all groups, though PTSD subjects had a greater level of grey matter volume (GMV) shrinkage compared to the other subjects, more specifically in the left hypothalamus, left inferior parietal lobule, frontal lobe, temporal lobe and cerebellum. The frontal lobe, in charge of a wide range of cognitive functions, when damaged, can lead to irritability, personality changes and impairment of decision making (Rosch and Mostofsky, 2019). Temporal lobe aids at processing sounds and thoughts and when damaged, not only it may lead to hearing loss, but also damages our ability to organize and sequence our behavior (Kiernan, 2012). Tests conducted on animals have linked fear conditioning to alterations in the cerebellum (Shin and Liberzon, 2010b). Examining the symptoms of fear and anxiety driven diseases, the team of researchers has been able to establish a direct link between GMR and OCD and PTSD, though they have also been able to observe physiological differences in these alterations between the tested groups.

Other studies conducted on neurocircuitry of OCD (Attwells *et al.*, 2017a) and PTSD (Speer, Upton, Semple and McKune, 2018) have shown inflammation to be a link to chronic diseases. In the body, inflammation is a biological response to harmful stimuli such as infections to chemicals and damaged tissue (Freire and Van Dyke, 2013). Earlier studies suggest that inflammation in the brain may also be a response to such harmful external stimuli; however, further research indicates that neuroinflammation could also be directly connected to diseases such as PTSD and OCD.

Research studies on genetic predisposition to anxiety and fear-based disorders

It has been proposed since the 20th century that genetic predisposition to anxiety and fear-based behaviour may be a contributor to the onset of certain mental diseases. One of the earliest studies conducted in London has examined the medical history of a group of subjects and found that over one third of 50 patients had had parents with OCD and nearly a quarter had siblings with diagnosed obsessive behaviour (Nestadt, Grados, and Samuels 2010). Another study seemed to have supported the hereditary nature of OCD where prevalence has shown primarily amongst first degree relatives, i.e. parents and siblings (Nestadt *et al.*, 2000). Subsequently, OCD has been observed to have the highest degree of concordance amongst monozygotic twins (MZ) at a rate of nearly 80% compared to dizygotic twins (DZ) at 50% (Kim and Kim, 2006). PTSD studies on siblings have also shown an increased occurrence amongst MZ twins and an overall 30% chance of a subject developing PTSD if the condition was already present in the family (Harvard Medical School, n.d.).

HYPOTHESIS AND OBJECTIVES

Current studies on neurological alterations of the brain in relation to mental health disorders are divided on the question of causality between neurological, anatomical and biochemical alterations and the development of mental health disorders like PTSD and OCD. It is the chicken and egg question that science has not yet been able to find an answer to beyond reasonable doubt. It is hypothesized that while GMR and swelling of brain tissue and blood vessels may occur as a response to traumatic life events or at the onset of severely compulsive behaviour, individuals that develop these disorders have already carried a genetic and neurological predisposition waiting for the right trigger to activate them.

In the light of the current situation, a literature review that examines some of the more recent discoveries about neural and brain alterations of patients with PTSD and OCD compared to the healthy population, more specifically the commonalities and differences in how inflammation and GMR accompany these conditions, will be useful for the establishment of factors – medical, behavioural, psychological and environmental – that must be considered in the adequate diagnosis of PTSD and OCD.

It is thanks to the brain that we are able to form memories, process thought and speech, make decisions that allow us to function normally in society, recognize danger and act upon that danger in a calculated manner. As such, the brain is a complex mechanism of interplay between over 80 billion neurons organized in areas and structures that support and complement each other so that a human being is able to process internal and external stimuli, apply healthy cognition and

behaviour and lead a normal life. Consequently, injury or damage to the brain leads to degeneration of brain cells and affects the daily life of survivors and their families (Stocchetti and Zanier, 2016)

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Secondary objectives:

Evaluate the correlation between OCD and PTSD, as well as their similarities and differences.

Analyse if brain alterations may impact directly the development and sustenance of OCD and PTSD

Evaluate if there is genetic predisposition to OCD and PTSD

Propose some considerations that may further the investigation of medical bodies into the conditions and circumstances that promote the development of OCD and PTSD, with the aim of identifying early signs before their onset.

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MATERIALS AND METHODS

A narrative literature review was conducted on research results that compare the impact and onset of inflammation and GMR on PTSD and OCD, the presence of genetic predisposition and the comorbidity between fear and anxiety-based disorders.

Search methods in selecting available literature

A number of databases with specialities including neuroscience, neuropsychology, mental health, psychiatry, cognition, cognitive neuroscience, etc. have been selected for adequate scientific and science-based material in order to collect reviews, reports and case studies pertaining to the topic of this literature review. These databases include ResearchGate, Cochrane Library, PubMed, PubMed Central, Frontiers in Behavioral Neuroscience, ScienceDirect, Healthline, Nature.

Keywords: PTSD, OCD, pro-inflammation, immune system, anxiety disorders, grey matter reduction, comorbidities, genetics, twins.

A database search was conducted selecting all words required in the search, the specific site or domain the search was conducted in and setting for the most relevant results to be shown.

Table 1.

Search results

Number of results per keywords	PubMed and PubMed Central	Cochrane Library	ScienceDirect
PTSD OCD Inflammation	269	11	44
PTSD OCD grey matter reduction	363	23	99
PTSD OCD comorbidity	1929	22	1273
PTSD OCD genetic predisposition	226	2	69
PTSD OCD twin studies	238	5	126

Given the high number of articles and publications, the selection was made by prioritizing the search results shown in the first page, articles that had a high number of citations and references cited by selected articles.

A Boolean search was conducted. E.g. OCD AND PTSD, brain AND alterations AND OCD Searches were conducted on topics not directly connected, however relevant to the research objective. E.g. role of the basal ganglia

A total of 15 to 20 articles and publications got reviewed per each topic which then was reduced to 43, which were found most relevant.

Inclusion and exclusion criteria

Inclusion criteria:

Scientific studies on GMR and inflammatory diseases linked to PTSD and OCD

Literature reviews of aforementioned scientific studies

Research papers comparing the symptomatology of PTSD and OCD

Genetic predisposition to PTSD and OCD

A comparison was drawn between the psychological and behavioural symptoms of OCD and PTSD and a connection was investigated to brain alterations in both diseases, specifically grey matter reduction and inflammatory diseases.

A connection was researched between OCD and PTSD and genetic inheritance amongst first degree family members, MZ and DZ twins.

Exclusion criteria:

Papers and publications focusing on therapy methods and psychological interventions have been considered irrelevant and disregarded in this review.

RESULTS

The review of some of the most recent studies has revealed clear evidence of the relation between chronically compulsive and fear-based behaviour and brain alteration. Research findings show that OCD, PTSD as well as other fear, anxiety or depression-based diseases may not necessarily coexist or co-create each other; however, patients suffering from one of these conditions are more likely to develop sometime during their lifetimes another mental disorder from the same or connecting families of disorders.

It has also become evident that alterations of the brain, specifically GMV reduction and neuroinflammation are common symptoms,

red flags, as well as accompanying conditions, though in a study of OCD, PTSD and SAD, MRI of PTSD brains have shown a greater degree of brain shrinkage than the other groups.

Lastly, close family members (parents, children and siblings) of diagnosed patients have been found to be significantly more likely to be predisposed or to have been diagnosed with OCD or PTSD.

Co-occurrence and symptomatology of OCD and PTSD

Prevalence of OCD and PTSD has been most extensively studied amongst war veterans and victims. Morina *et al.* (2016) conducted a study of civilian surviving victims of the Kosovo War searching for evidence of OCD and PTSD symptoms as well as the interconnectedness of these two diseases. They found that 39% were showing symptoms of stress, fear and anxiety and a significant number of subjects tested for either disorder were also predisposed to carry the symptoms of the other. Compared to the general population, a PTSD brain is 47% more likely to develop OCD and patients with obsessive compulsions had an up to 52% likeliness of having had a traumatic event in their life prior to developing OCD. Researchers conducted a Posttraumatic Diagnostic Scale (PDS) questionnaire, an Obsessive-Compulsive Inventory (OCI-R) questionnaire and a Hopkins Symptom Checklist to test for signs of depression. Gender was found to play a significant role in the likeliness of developing obsessive-compulsive symptoms, with 47% of women with a traumatic past event likely to also experience obsessive compulsions, while only one out of four men reported the same. Type and number of traumatic events as well as depression were found not to significantly impact the development of PTSD with either gender. Education was negatively correlated to mental health issues.

Though multiple studies have confirmed the co-occurrence of PTSD and OCD, it is important to remember that as much as these two debilitating mental diseases co-exist or aggravate each other's symptoms, there are differences scientists and therapists must observe both for accurate diagnosis, as well as for the purpose of applying the adequate medicinal and psychotherapeutic treatments. PTSD and OCD are both characterized by intrusive negative thoughts that may range from absent mindedness, through depressive outlook to the world to aggression towards oneself or others. Both conditions are experienced as an inability to take control of one's life, thoughts and emotions, triggering erratic, unusual behaviour and mood swings. In both cases, the onset of the symptoms may be sudden, may develop gradually with the early symptoms going unnoticed both for the subject and their family and they may get triggered and activated much later, for example as a delayed response to childhood trauma (McFarlane, 2010b) making it difficult to identify what may have caused them.

In terms of differences, it was found that the focus of an OCD brain is on a future behaviour or experience, while a PTSD subject is taken back compulsively to the past, reliving over and over the details of their trauma. This directional difference is largely the driver behind the behaviours. OCD patients establish rituals as a means of preventing an imagined threat from happening, despite intellectually being aware that the repetition on its own will not

bring the desired outcome or remove the threat. The compulsion however outlaws rationale. Avoidance of triggering circumstances may also be present as a means of sustaining a sense of control. PTSD patients on the other hand avoid situations and people that remind them of the experienced trauma, even when consciously they may be aware of the lack of any connection to the pain they suffered in the past. The repetitive behaviour as such is directed at diminishing and eliminating circumstances and conditions that may take them back to the experience of their trauma. Given the comorbidity of PTSD and OCD and the lifetime prevalence of PTSD ranging from 1% to over 9% in lower-middle to upper-middle income countries (Sareen, 2014) it is perhaps of no surprise that OCD is sometimes developed as a coping mechanism for someone suffering from past trauma they have not been able to overcome (Dinn, Harris and Raynard, 1999).

Findings of brain alterations in OCD and PTSD

The aforementioned study by Cheng *et al*. (2015) has conducted MRI scans on 3 groups, 30 PTSD subjects, 29 with OCD and 20 with SAD against 30 healthy controls (HC). Brain alterations have been identified in all 3 groups, however in different brain areas and to different degrees.

With the use of VBN technique (Nemoto, 2017) they have examined focal brain differences. That is to say, even though no two brains are exactly the same, healthy brains have the same anatomy, same volume of areas proportionate to the total brain mass, same neurocircuitry and so on. Images obtained with VBN allowed them to see which areas of the brain showed neuroanatomical alterations compared to a healthy brain, the OCD brain vs the PTSD and SAD brain, as well as compared to the rest of the subjects' own brain. Researchers found that age played no role in the differentiation of the 4 groups. Some of the most evident differences have been observed in the left hypothalamus and left inferior parietal lobule (IPL). The hypothalamus in conjunction with the pituitary gland plays a key role in a number of functions, such as hormone release, temperature control of the body, regulation of emotional response to external and internal stimuli (Flament-Durand, 1980). When damaged, a dysfunction of these roles alone is sufficient to throw off the immune system, cause irregular body temperature and neuroinflammation and alter the patient's ability to assess and apply appropriate emotional response.

The inferior parietal lobule (IPL) located in the left hemisphere of the brain carries a multimodal property in the sense that it acts as a point of junction and translator of different stimuli, such as visual, sensorimotor, auditory, language, etc. and our brain's ability to classify and organize things, as well as maintain focus on the task at hand are largely dependent on it (Singh-Curry and Husain, 2009). When damaged, we damage an area responsible for perspective thinking. Arora *et al.* (2015) argued, that when faced with the need of changing our perspective about something, whether that need is triggered by internal thoughts or external stimuli, due to their exogenous nature these stimuli should prompt an activation of IPL. In case of neural degeneration of this area, the ability to identify thoughts and behaviour that serve the individual may be lost. While an OCD brain is typically able to recognize harming

or unwanted behaviour and its main challenges lie in its inability to control it or prevent acting on it, for a PTSD subject the difficulty is in gaining perspective of the entirety of their life and the person is instead consumed by the details and impact of the trauma they suffered.

Inflammation in the OCD and PTSD brains

Hori and Kim's study (2019) postulates that:

Epidemiological studies have demonstrated that PTSD is associated with significantly increased rates of physical comorbidities in which immune dysregulation is involved, such as metabolic syndrome, atherosclerotic cardiovascular disease, and autoimmune diseases. In line with this, a number of blood biomarker studies have reported that compared to healthy controls, individuals with PTSD exhibit significantly elevated levels of proinflammatory markers, such as interleukin-1β, interleukin-6, tumour necrosis factor-α, and C-reactive protein (p. 143).

It was further proposed that PTSD is connected to physical diseases apparently non-related to the brain, such as obesity, diabetes, autoimmune disease and cardiovascular diseases. These conditions however are known to have inflammatory properties. Interleukin-6 (IL-6) acts both as a pro and anti-inflammatory interleukin, which in this case further complicates matters (Tanaka, Narazaki and Kishimoto, 2014). Patients with PTSD have consistently shown increased levels of pro-inflammatory markers, however the IL-6 in combination with other biomarkers have also generated inflammatory markers below the control groups. Temporality between the occurrence of PTSD and inflammation offers an additional source of debates and poses the need for further research. If inflammation aids the dysregulation of the immune system as well as the development of stress, depression, lack of clarity of thought, etc. it becomes easy to understand how it can also be a contributing factor to the onset of PTSD. Other studies however conducted on women with PTSD have not been able to identify conclusive evidence that there may have been significant differences in the levels of pro-inflammatory markers in those who have been diagnosed with the disease and the healthy control groups.

A study by the Centre for Addiction and Mental Health (CAMH) may be the first to showcase evidence of the relationship between OCD and inflammation, specifically that certain brain areas function differently in OCD (O'Malley, 2017). This poses the inevitable question of how the brain in its entirety works. That is to say, is there a predetermined set of rules and regulations that warrant a healthy normal functioning of this important organ and diseases are the cause of glitches in the system, or is it the alteration from the norm that makes room for diseases to develop? In a case-control study by Attwells *et al. (2017b)* researchers examined the presence of neuroinflammation in the basal ganglia. The basal ganglia is closely connected to a number of brain areas, including the thalamus. Besides its role in motoric functions, the basal ganglia also play an important role in the regulation of emotions and cognitive functions (Lanciego, Luquin and Obeso, 2012). The thalamus and hypothalamus are part of the diencephalon, which acts as a relay of sensory information and connects the nervous system and endocrine system. When dysregulated or under attack, the affected areas appear to produce an autoimmune-like response to

infection. Positron emission tomography (PET) radioligands have been connected to translocator protein (TSPO) with the aim of finding evidence that neuroinflammation causes an increased translocation protein density at the point of microglial activation. Microglial cells act as mediators in the central nervous systems' (CNS) immune response to infections and inflammations. Though certain limitations have been identified in the use of PET scans and the interpretation of the data, the results have shown clear evidence that when microglial cells are activated, symptoms of OCD, such as distress and anxiety levels have also increased in concordance with greater TSPO distribution volume (V_T) in the orbitofrontal cortex (Setiawan, *et al.,* 2015).

Twins carry the evidence of genetic predisposition

The study by Nestadt *et al.* (2010) postulates the existence of genetic contribution to the aetiology of OCD. Besides the biological components (commonality of compulsive behaviour in a number of psychiatric conditions such as Tourette syndrome, schizophrenia, Parkinson's disease, etc., as well as prevalence of altered metabolic activity in brain areas involved in higher cognition and regulation of emotions) it has been observed that a significant number of OCD subjects had the condition running in the family. Different family studies have produced different results on occurrence of OCD amongst first degree relatives. An earlier research by Lenane *et al.* (1990) on young subjects reported a 7% to 15% chance of the child developing OCD if they had a parent or a sibling diagnosed with the condition or showing symptoms of the diseases. A later study by do Rosario-Campos *et al.* (2005) observed a 32.5% ratio. Though the two studies report significantly different ratios, something that could be attributed to questionnaires increasing in precision over time, or to the development of our understanding of the condition by scientific bodies, they are very similar in that onset at an early age is a strong indicator of genetic inheritance. First tests on twins date back to the 1930s (Lewis, 1936) and since then scientists have allocated a special attention to this subgroup, which at an 80% prevalence amongst MZ twins comes to no surprise. Serotonin has been closely linked to OCD, as it plays an important role in the communication between different parts of the brain. When the serotonin transporter called the SERT gene is impacted, it contributes to the breakdown of the communication (Murphy, Lerner, Rudnick, and Lesch, 2004). As such, serotonin studies have been the focal point of research in a context where amongst twins and siblings the serotonin transporter coding variant was suspected to have been increased by the close genetic similarity. Despite of clear evidence of genetic predisposition and inheritance of OCD between close family members and twins, the less than 100% prevalence amongst MZ twins is also an indicator of the role of both nature and nurture, in other words environmental factors also playing an important role in the likeliness of someone developing compulsive disorders (Hemmings and Stein, 2006).

According to the American Psychological Association (APA), "Trauma is an emotional response to a terrible event like an accident, rape or natural disaster. Immediately after the event, shock and denial are typical" (Berman, 2019). The WHO World Mental Health (WMH) surveyed 24 countries for a total of 29 different types of lifetime and

randomly selected traumas with the aim of identifying a link between PTSD and different traumatic event types (Kessler *et al.*, 2017). A total of 68,894 adult subjects were interviewed twice, once for a significant life altering trauma and a second for a random trauma type, evaluated as less likely to mark for lifetime. Over a staggering 70% of the respondents reported having experienced or witnessed a traumatic event and over 30% exposed to four or more. Yet according to the World Health Organization (WHO) statistics, less than 4% of the population of the world suffers from PTSD (WHO, 2013). Though these numbers vary across geographies, genders and cultural groups and statistics change as more data is collected, they pose the question of why and how only a relatively small percentage of people exposed to traumas develop a mental health disorder as their consequence. Research shows that predisposition to anxiety, stress, fear and depression tend to run in the family. Cornelis *et al.* (2010) points out that while genetics have been long observed to play a role in the development of PTSD, the genetic variants that may act as a root cause are still in question. Much like with OCD, PTSD studies with MZ and DZ twins have shown a 30% to 40% probability of inheritability compared to the general population. Predisposition to PTSD has been tested from the perspective of heritability of PTSD and heritability of traumatic events. Studies have shown that the human body is an active participant in the selection and processing of the environmental stimuli (Kremen, Koenen, Afari, and Lyonse, 2011). That is to say, in a process called gene-environment covariance (Kendler and Eaves, 1986) the human organism makes choices of what it wants to get exposed to and what stimuli or circumstances will get filtered out. In the 60s psychologists have stressed the importance of a person's role in shaping their environment, instead of just being a passive receiver of their circumstances. By the 70s the focus has shifted through twin studies to the role of genetics and over the decades an increasing amount of evidence was collected on "the causal mechanisms, which indicate genetic control over environmental exposure" (Jaffee and Price, 2007). As such, heritability of PTSD, similarly to vulnerabilities to other disorders amongst twins has provided and continues to provide scientists areas of research that bring us closer to an understanding of underlying biological and genetic mechanisms of inheritable mental and physical conditions.

DISCUSSION

Interpretation

The review aimed at gathering research-based evidence of a few aspects of PTSD and OCD from the perspective of brain alterations, neuroinflammation and genetic heritability. As postulated in the hypothesis, the biochemistry of the brain offers a complex web of information directly linked to mental health. A regulated communication between brain cells and the rest of the body helps our ideal functioning as human beings; however, when dysregulated, this complex system becomes vulnerable and triggers changes in our behaviour, thinking, information processing, the ability to manage our emotions and so on. Grey matter reduction can be both a symptom and a consequence. Alteration of the brain is prevalent in a number of neurodegenerative diseases, some directly linked to aging and unrelated to trauma or obsessive compulsions. With nearly three quarters of

the world's population exposed to trauma, it is perhaps a possibility that trauma doesn't just simply get erased from our lives, but finds alternate routes of manifesting through physical or psychological issues. Neuroinflammation is another aspect that research shows to be undoubtedly linked to mental health conditions. But it is also a commonality in diabetes, obesity, asthma or Alzheimer's disease. This makes the connection evident, yet not exclusive. Lastly, twin and first-degree family studies carry sufficient data to warrant further studies into the role of genetics, environment however has also proven to play a significant role.

Implications and Recommendations

Almost every reviewed piece of research and literature has highlighted as a shortcoming the lack of sufficient data, case studies and general evidence that could position science into a place of certainty about causes and consequences, as well as a precise diagnosis of OCD and PTSD, or the symptoms and circumstances that accompany them. This review is no different. Compared to a few hundred years ago our knowledge is immensely greater than it was before. Yet there is so much more left to be understood. Current evidence suggests that we carry certain predispositions that impact the way we shape our reality, even in the case of unexpected traumatic events. However, if there was transgenerational trauma, one must wonder if it is a genetic or a memory imprint that makes us what and how we are.

As we discussed earlier, women are more prone to develop fear or anxiety-based disorders than men. The reasons are outside the topic of our research; however, understanding the neuro-bio-chemical differences between a female and male brain could shed some light on the mere definition of trauma or compulsion and bring us closer to understanding why for such a relatively small percentage of people, exposure to traumatic events culminates in the development of mental disorders as we define them today. It would therefore be important to increase the number of gender specific research.

Another limitation of currently available research relates to the topic of prevention. To the best of our knowledge, there is no material that speaks in practical terms of measures that could be taken to avoid developing OCD or PTSD, or reliable signs that would forecast their onset. How could prevention even be a possibility, one might ask. This review has referenced data that showcases biochemical and genetic implications of both disorders. We do know that evidence is available, albeit not collected in sufficient quantities and when data is harvested, is at a stage where the disorder has already developed. Similarly, questionnaires gather information on signs and symptoms of existing conditions, but since we know that gene-environment covariance has a direct impact on the choices our physical and biological organisms make, establishing the pre-symptomatic signs could lead us a step closer to addressing these diseases before their onset. As such the call for participation in studies and questionnaires must place more focus on gender studies, children and general population, alongside high probability groups, such as war veterans; investigations must expand beyond the obvious victim groups.

CONCLUSIONS

Research findings showed that family and twin studies offer conclusive evidence of genetic heritability and the neurochemistry and anatomical changes of our brain provide insight into how OCD and PTSD are developed. And yet the chicken and egg question remain open.

Religions, sciences, therapy, behaviourism, spirituality, environmentalism have all tried and continue to try finding answers to how we operate. What triggers and motivates us, what factors drive our decisions, why we have different responses to the same situation, why we interpret life events, thoughts and emotions in so many different ways. Emergence of new trends, the rapid development of technology, medical, pharmacological and scientific discoveries, globalization of available knowledge have all contributed massively to our current understanding of mental health, yet none of them individually or collectively have been able to articulate a bullet proof solution that answers all questions.

This literature review was conducted with an appreciation of the fact that there will be more questions than answers. As such, it was meant to synthesize some of the currently available trends and knowledge on PTSD and OCD from the perspective of their symptomatology, co-occurrence and genetic and biochemical underlying causes; it was further meant to propose new areas of investigation.

A holistic approach to mental diseases is paramount. Our body and mind when optimal, operate in harmony. When dysfunctional, our whole being is impacted. We must not assume that drugs alone are sufficient to reduce inflammation or take away a headache. We must also not assume that weeks and months spent in behaviour therapy holds alone the key to our wellbeing. Genetic predisposition has been proven time after time to be a significant contributor to the things we are prone to, however environment also plays an important role, as countless family studies support that. There is also no one size that fits all. As such, this review proposes to professionals working in the health industry reflection on the limitations they have in their expertise, openness to integrate in their practice areas complementing their speciality and willingness to see and treat every case they come across as an opportunity to broaden their knowledge.

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