Morbidity and mortality in obsessive-compulsive disorder: A narrative review

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ARTICLE INFO

Keywords:
Obsessive-compulsive disorder
Morbidity
Somatic health
Autoimmune diseases
Metabolic syndrome
Cardiovascular diseases
Dementia
Sleep disorders
Respiratory diseases
Gastrointestinal diseases
Migraine
Chronic pain
Mortality
Suicide

ABSTRACT

Current knowledge on the general somatic health of individuals with obsessive-compulsive disorder (OCD) is very limited. Here, we critically review the emerging literature on the topic. Rapidly accumulating evidence indicates an association between OCD and autoimmune diseases, which is not limited to streptococcus-related conditions. Similarly, an association with metabolic and circulatory system diseases has been reported, which is at least partially independent from psychiatric comorbidities and familial confounders. Preliminary results also suggest potential links with dementia, insomnia, respiratory diseases, gastrointestinal diseases, migraine, and chronic pain, but replication is warranted. The risk of death by suicide in OCD is now well established. OCD has also been associated to increased mortality due to natural causes, but more research on specific causes of death is needed. Clarification of the mechanisms behind the observed associations will be critical to inform the rational design of prevention efforts. In the meantime, while OCD symptom reduction remains a priority, clinicians should also focus on monitoring the general health and promoting healthy lifestyles of persons with OCD.

1. Introduction

Obsessive-compulsive disorder (OCD) is a chronic and often debilitating psychiatric condition with a prevalence of 1–2% (Fawcett et al., 2020; Ruscio et al., 2010). OCD is usually accompanied by a range of psychiatric comorbidities, substantially reduced quality of life (Braakoulas et al., 2017; Ruscio et al., 2010), and long-term socio-economic adversity (Pérez-Vigil et al., 2018, 2019). Like in other psychiatric disorders (Momen et al., 2020), there is increased awareness that OCD may also be associated with a range of general medical conditions and premature mortality. An increased focus on the somatic health of individuals with OCD and the mechanisms behind these associations can eventually help reducing morbidity and mortality in this group. As the field moves to view OCD as a disorder with an impact on the health of the individual “as a whole” (Mataix-Cols et al., 2020), it is timely to summarize the current knowledge on the general health of individuals with OCD. Given the scarcity of literature on the topic, we conducted a narrative review of the literature in order to provide a time-efficient overview of the emerging evidence and identify knowledge gaps. Because the field is in its infancy, our review focuses primarily on areas where a substantial body of evidence has accumulated in recent years.

2. Autoimmune diseases

Autoimmunity has long been proposed to be potentially important in the etiology of a range of neuropsychiatric disorders, including OCD (Isung et al., 2020). A widely discussed model of autoimmunity postulates that OCD and related phenotypes like tics may arise in a similar way to Sydenham’s chorea, the neurological manifestation of rheumatic fever (Swedo, 1994; Swedo et al., 1998). According to this still-debated model, obsessive-compulsive symptoms (OCS) might be a consequence of an autoimmune reaction to group A beta-hemolytic streptococci...
of streptococcus-related conditions. Preliminary evidence suggests that there may be shared familial risk factors, genetic predisposition, and related conditions were significantly more common among Brazilian study (Hounie et al., 2007; Seixas et al., 2008) found that OCD individuals with first-degree relatives with autoimmune disorders, independent of either rheumatic fever or Sydenham’s chorea in another family member (Seixas et al., 2008). In another clinician-based study (Murphy et al., 2010), the mothers of 107 children and adolescents with OCD and/or tics were interviewed regarding their history of autoimmune diseases. Nearly 18% of the mothers reported at least one autoimmune disease; this figure was higher for the mothers of children fulfilling likely criteria for Pediatric Autoimmune Neuropsychiatric Disorder Associated with Streptococcal Infection (PANDAS) (n = 40; 25%), compared to the mothers of children with unlikely PANDAS (n = 67; 13.4%). In the above-mentioned population-based study from Sweden (Mataix-Cols et al., 2018), individuals with OCD were significantly more likely to have first-degree relatives with autoimmune disorders, independent of OCD status. In the American study by Westwell-Roper et al., first-degree relatives of individuals with OCD reported similarly elevated rates of scarlet fever, rheumatic fever, and encephalitis or meningitis, independent of OCD status (Westwell-Roper et al., 2019).

In sum, OCD is associated with a range of autoimmune diseases, not limited to streptococcal-related conditions. Preliminary evidence suggests that the association may be strongest in the subgroup meeting criteria for PANDAS or Pediatric Acute-onset Neuropsychiatric Syndrome (PANS) (Gromark et al., 2019, 2021; Murphy et al., 2010). Family studies suggest that there may be shared familial risk factors, genetic and/or environmental, between OCD and autoimmune diseases.

3. Cancer

Cancer has rarely been studied as an outcome in OCD. In a Taiwanese cohort of 52,656 individuals newly diagnosed with OCD (Shen et al., 2016), the incidence of cancer diagnoses during a 5-year follow-up period was compared with the expected national cancer incidence. Results showed a non-significant standardized incidence ratio (SIR) of all cancers in OCD (SIR =1.05, 95% CI 0.98–1.13). Nonetheless, an increased risk was observed within the first year of OCD diagnosis (SIR =1.21, 95% CI 1.01–1.43), which was hypothesized to be related to surveillance bias, by which individuals with OCD are likely to have more doctor appointments, leading to an earlier cancer detection. Regarding specific cancer sites, and after excluding patients with a cancer diagnosis within the first year of OCD diagnosis, a higher risk of hematologic, blader, and prostate cancers was noted among men with OCD, and a lower risk of uterine cancer was described in women with OCD; however, cancer-site results were based on smaller numbers and should be interpreted cautiously (Shen et al., 2016). In two waves of the survey-based Singapore Mental Health Study (Chong et al., 2012; Subramaniam et al., 2020), individuals with OCD, compared to those without, did not show an increased likelihood of self-reported cancer diagnoses. To our knowledge, no studies have focused on cancer mortality in OCD; thus, it is unclear if it is elevated in OCD, as described for individuals with psychiatric disorders in general (Kisely et al., 2013, 2016).

4. Circulatory system diseases

Three nationwide register-based studies have reported significant associations between OCD and metabolic, cardiovascular, and cerebrovascular conditions. In the first, Isomura et al. (2018) compared 25,415 individuals with OCD with more than 12 million individuals from the Swedish general population and to their unaffected full siblings. In both comparisons, OCD was associated with an increased risk of any metabolic or cardiovascular complication (HR =1.45, 95% CI 1.42–1.49 and HR =1.47, 95% CI 1.40–1.54, respectively). The risks were highest for obesity, type 2 diabetes, and circulatory system diseases, including hypertension and a broad range of cardiovascular diseases. The risks remained largely unchanged when accounting for different groups of psychiatric comorbidities. Interestingly, and compared with patients who were not taking serotonin reuptake inhibitors, individuals with OCD who were taking higher doses of serotonin reuptake inhibitors and who had a longer duration of treatment had significantly lower risks of metabolic and cardiovascular complications, regardless of whether they were also taking antipsychotics. This contrasts with previous findings from randomized controlled trials (Maina et al., 2008; Simpson et al., 2013; Skapinakis et al., 2007). Isomura et al. (2018) speculated that patients on medication may represent an inherently different group than those not taking medications, and that patients on medication are probably more likely to have access to more frequent follow-ups and a better management of their general health. The second study, conducted by the same group, focused on specific cardiovascular diseases (Isomura et al., 2021). Compared to controls, individuals with OCD (n = 33,561) had a 25% increased risk of any type of cardiovascular disease. The associations were strongest for the subtypes venous thrombo-embolism and heart failure. The results were again similar in the sibling comparison and were independent from other psychiatric and somatic diseases. The third study, done in Taiwan, focused specifically on risk of stroke (Chen et al., 2021) and found a significantly increased risk of ischemic (but not hemorrhagic) stroke in individuals with OCD (n = 28,064), compared to general population controls (HR =3.02, 95% CI 1.91–4.77). In this study, neither short- nor long-term use of antidepressants correlated with any of the outcomes.

Although several population surveys from Germany and Singapore did not find significant associations between OCD and self-reported cardiometabolic disorders (Chong et al., 2012; Subramaniam et al., 2020; Witthaeuer et al., 2014), the findings of a number of clinic-based studies are in line with those of the nationwide register-based studies from Sweden and Taiwan. In an investigation including 104 individuals with OCD at an Italian outpatient clinic, 21.2% presented with metabolic syndrome (Albert et al., 2013). Metabolic syndrome was associated with a longer lifetime exposure to antipsychotic medication (Albert et al., 1994; Swedo et al., 1998). The hypothesized molecular mechanisms, evidence, and controversies surrounding this model are covered elsewhere (Cunningham, 2014; Gilbert, 2019). A body of work has focused on the co-occurrence of autoimmune diseases and OCD (see Pérez-Vigil et al., 2016) for a review. A population-based study in Taiwan compared 63,165 individuals with systemic autoimmune diseases to 315,825 unaffected individuals. A higher incidence of subsequent OCD was found in the autoimmune disease group (hazard ratio [HR] =1.85, 95% confidence interval [CI] 1.41–2.43). Specifically, the risk of OCD was significantly higher in individuals with dermatomyositis, Sydenham’s syndrome, and systemic lupus erythematosus (Wang et al., 2019). Similarly, a population-based study from Sweden found that individuals with OCD (n = 30,882) were 43% more likely to have an autoimmune disease, compared to unaffected individuals from the general population (Mataix-Cols et al., 2018). Increased odds of most individual autoimmune diseases in patients with OCD were reported, including Sydenham’s syndrome, celiac disease, Guillain-Barre syndrome, Crohn’s disease, Hashimoto’s thyroiditis, type 1 diabetes, scarlet fever, idiopathic thrombocytopenic purpura, ulcerative colitis, multiple sclerosis, and psoriasis vulgaris. Another study including 1401 individuals with OCD and their 1045 first-degree relatives from the OCD Collaborative Genetics Association Study (Westwell-Roper et al., 2019) found that diagnosed individuals had higher-than-expected prevalence of self-reported scarlet fever, encephalitis or meningitis, rheumatoid arthritis, and rheumatic fever, but not systemic lupus erythematosus, diabetes, asthma, multiple sclerosis, psoriasis or inflammatory bowel disease. However, this study lacked a control group.

Family studies have also suggested that the first-degree relatives of individuals with OCD have elevated rates of autoimmune diseases. A Brazilian study (Hinnie et al., 2007; Seixas et al., 2008) found that OCD and related conditions were significantly more common among first-degree relatives of individuals with rheumatic fever than among first-degree relatives of controls (14.7% vs. 7.3%) (Hinnie et al., 2007), and the risk of OCD and related disorders was increased by the presence of either rheumatic fever or Sydenham’s chorea in another family member (Seixas et al., 2008). In another clinic-based study (Murphy et al., 2010), the mothers of 107 children and adolescents with OCD and/or tics were interviewed regarding their history of autoimmune diseases. Nearly 18% of the mothers reported at least one autoimmune disease; this figure was higher for the mothers of children fulfilling likely criteria for Pediatric Autoimmune Neuropsychiatric Disorder Associated with Streptococcal Infection (PANDAS) (n = 40; 25%), compared to the mothers of children with unlikely PANDAS (n = 67; 13.4%). In the above-mentioned population-based study from Sweden (Mataix-Cols et al., 2018), individuals with OCD were significantly more likely to have first-degree relatives with autoimmune disorders, independent of OCD status. In the American study by Westwell-Roper et al., first-degree relatives of individuals with OCD reported similarly elevated rates of scarlet fever, rheumatic fever, and encephalitis or meningitis, independent of OCD status (Westwell-Roper et al., 2019).

In sum, OCD is associated with a range of autoimmune diseases, not limited to streptococcal-related conditions. Preliminary evidence suggests that the association may be strongest in the subgroup meeting criteria for PANDAS or Pediatric Acute-onset Neuropsychiatric Syndrome (PANS) (Gromark et al., 2019, 2021; Murphy et al., 2010). Family studies suggest that there may be shared familial risk factors, genetic and/or environmental, between OCD and autoimmune diseases.
6. Gastrointestinal diseases

In the 1998 German Mental Health survey (Withthauer et al., 2014), gastrointestinal diseases (ulcer, gastritis) were more frequent in the group with OCD compared to those without OCD, while allergies were not. The survey-based Singapore Mental Health Study reported a significant association between OCD and self-reported respiratory conditions (including asthma, among others) in its 2010 wave (Chong et al., 2012), but failed to find a significant association between OCD and asthma only in the 2016 wave (Subramaniam et al., 2020).

In the OCD Collaborative Genetics Association Study (Westwell-Roper et al., 2019), including 1401 OCD cases, the lifetime prevalence of asthma was within the range expected in the general population. A Turkish study compared young people (ages 6–18) diagnosed with OCD only (n = 13), Tourette syndrome only (n = 9) or both (n = 13) to 35 controls (Yuce et al., 2014). The OCD only and OCD plus Tourette syndrome groups had a significantly higher frequency of any allergic disease (61.5% in both groups), including asthma, allergic rhinitis, and eczema, compared to controls (22.9%). Those with both disorders also presented with higher frequencies of eczema and higher rates of positive skin prick tests to measure atopy, compared to controls.

Other studies explored the prevalence of OCD in samples of asthma patients. Valença et al. (2006) reported that 3.2% of 62 individuals at two asthma clinics in Brazil met OCD criteria. In the sample of 24 individuals from an asthma center in Canada described by Paquet et al. (2019), 16.7% had OCD. To summarize, the literature on the association between OCD and respiratory diseases and allergies is inconsistent and methodologically limited.

6. Gastrointestinal diseases

In the 1998 German Mental Health survey (Withthauer et al., 2014), gastrointestinal diseases (ulcer, gastritis) were more frequent in the group with OCD compared to those without OCD, although this difference was not statistically significant. In a population survey from 2010 in Singapore (Chong et al., 2012), individuals with OCD had a significantly higher proportion of stomach ulcer, chronic inflammatory bowel, enteritis or colitis, compared to those without OCD. However, in the 2016 wave (Subramaniam et al., 2020), there were no between-group differences in the frequency of ulcer (the other conditions were not explored). In the above-mentioned Italian study including 162 outpatients with OCD (Aguglia et al., 2018), 20.5% presented with upper/lower gastrointestinal diseases. The most frequent conditions within this group were gastroesophageal reflux (15.4%), Gilbert’s syndrome (6.2%), and chronic inflammatory infectious diseases and cholelithiasis (4.3%).

Some studies have focused specifically on OCD and irritable bowel syndrome (IBS). Among 37 US-individuals diagnosed with OCD (Masand et al., 2006), 35.1% met criteria for IBS, compared with 2.5% of matched controls (n = 40). A higher prevalence of IBS was also found in a Canadian study including 21 OCD cases and 22 controls (47.6% vs. 4.5%, respectively) (Turna et al., 2019). In a sample of 120 Iranian patients with IBS, 18 (15%) had OCD (Davarinejad et al., 2021). These results contrast with those reported in another Canadian study of 50 individuals with OCD whose frequency of IBS was comparable to the community rates (Gros et al., 2009). In sum, the available evidence on the potential association between OCD and gastrointestinal disorders is scarce and based on small samples, leading to mixed results. Further studies on the prevalence of gastrointestinal disorders in OCD, as well as the clinical correlates and mechanisms of association, are warranted.

7. Neurological disorders

A limited number of studies have examined associations between OCD and neurological disorders. In a Taiwanese register-based study, Chen, Cheng et al. (2021) showed that individuals with OCD older than 44 years (n = 13,470), compared to matched controls (n = 13,470), had a higher risk of developing dementia during the study period (87 vs. 124 new cases, respectively; HR = 4.28, 95% CI 2.96–6.21), with an average age at onset of dementia about 6 years younger. The risks were highest for unspecified dementia, followed by Alzheimer’s disease and vascular dementia. However, this study did not take comorbid depression into account, which is one of the most frequent comorbidities in patients with OCD and could be a potential confounder in this association (Diniz et al., 2013).

In a meta-analysis of seven studies (n range=50–188), the pooled prevalence of OCD in individuals with epilepsy was 2.4% (95% CI 1.6–3.7%) (Yang et al., 2020). Although there were no control groups without epilepsy, the prevalence of OCD in the general population (Fawcett et al., 2020; Ruscio et al., 2010) falls within this confidence interval, rendering the results inconclusive.

Significant associations between OCD and migraines have been reported in community surveys from the US (Breslau et al., 1991), Brazil (Goulart et al., 2014), Singapore (Jayagurunathan et al., 2020), and Germany (Withthauer et al., 2014), but not in another US-based survey (Swartz et al., 2000). A handful of clinical-based studies have explored the prevalence of OCD in individuals with headaches and migraine (Beghi et al., 2010; Cupini et al., 2009; Pavone et al., 2012). In line with some of the survey-based studies (Breslau et al., 1991; Goulart et al., 2014), these clinical examinations point out to stronger associations between OCD and the most severe cases; for example, those with both migraines plus tension-type headaches, compared to either separately (Beghi et al., 2010), and those with medication-overuse headache and chronic migraines, compared to those with episodic migraines, chronic migraines, and controls without headaches (Cupini et al., 2009). In a pediatric study (Pavone et al., 2012), the prevalence of OCD in children with primary headaches was not significantly higher than in the controls. However, OCD showed to be significantly more frequent in children with migraines vs. tension-type headaches.

In sum, the literature suggests a potential association between OCD and dementia and headaches and migraines that will require replication. The association between OCD and epilepsy is unclear.

8. Sleep problems

The literature on OCD and sleep difficulties has previously been summarized in a number of systematic reviews and/or meta-analyses (Cox et al., 2020; Diaz-Roman et al., 2015; Nota et al., 2015; Paterson et al., 2015; Perera et al., 2019).

The meta-analysis by Diaz-Roman et al. (2015) included four polysomnography (PSG) studies, totaling 111 individuals with OCD and 141 controls. The results showed that individuals with OCD, compared to controls, had shorter total sleep time, spent more time awake, had less sleep efficiency, and spent less time in stage 2 of sleep. When participants with comorbid depression were excluded, only reduced sleep latency remained significant.
The meta-analysis by Nota et al. (2015) included 12 studies (7 using PSG, 3 using self-reported data, and 2 using information from a third party), totaling 404 OCD cases and 231 controls. They examined six sleep-related disturbances and reported the largest effect for the prevalence of self-reported delayed sleep phase disorder (DSPD), which was higher in those with OCD than in the controls. The prevalence of DSPD was also examined in a more recent study by Coles et al. which, in line with the meta-analytical results, showed that 42% of their 24 individuals with OCD met the criteria for DSPD, compared to 0% of the control sample (Coles et al., 2020). The other parameter that showed significant effects in the meta-analysis by Nota et al. (2015) was the duration of sleep, which was shorter in OCD cases, compared to controls, similar to the finding reported by Diaz-Roman et al. (2015) (which included overlapping studies). When studies with individuals with comorbid depression were excluded, results still held, indicating that the two significant differential effects (prevalence of DSPD and duration of sleep) could not be attributed to the presence of comorbid depression (Nota et al., 2015).

In general, the literature on OCD and subjective assessment of sleep problems includes multiple limitations. Studies have been generally small, assessment measures are often heterogeneous and based on self-report and the role of psychiatric comorbidities on the associations is unclear. In the largest study to date on sleep problems in OCD, Sevilla-Cermeño et al. (2020) addressed some of these limitations by examining the prevalence of insomnia in a Swedish population-based study of more than 13 million individuals, including 31,856 with OCD. Insomnia cases were ascertained by selecting individuals with a clinical diagnosis made by a specialist physician or those who were dispensed a drug with specific insomnia indication. Results showed that 42.2% of individuals with OCD and 11.0% of the general population had insomnia, translating into a 7-fold increased odds of insomnia in OCD. A sibling comparison produced a slightly reduced but still largely significant estimate (5-fold increased odds), indicating that familial factors did not fully explain the association. Comorbid depressive and anxiety disorders also accounted for part of the risk, but did not fully explain it. Other smaller studies including control groups echo the results of the Swedish epidemiological findings in insomnia and expand these results to include other types of sleep disturbances (Bobbey et al., 2002; Donse et al., 2017; Ivarsson and Larsson, 2009; Jaspers-Fayer et al., 2018; Ramsawh et al., 2009).

In sum, these previous works – focused on both objective (i.e., polysomnography, actigraphy) and subjective sleep-related measures – suggest an association between OCD and electrophysiological abnormalities and sleep disorders across the lifespan. However, larger and methodologically sound studies are still needed.

9. Chronic pain

Results from survey-based population studies suggest an association between OCD and pain. Two waves of the Singapore Mental Health Study (Chong et al., 2012; Subramaniam et al., 2020) showed significant associations between OCD and chronic pain (including arthritis, back and spinal disc issues, headaches, migraine, and rheumatism). In a German study (Beesdo et al., 2010), 36 of the 38 individuals with OCD self-reported lifetime significant pain symptoms. In the US-based 2004 National Nursing Home Survey (Walid and Zaytseva, 2009), 18.3% of 5063 residents with OCD reported pain and, compared to residents with other psychiatric disorders or dementia, the OCD group reported the highest pain intensities. Finally, in a US-study including only women (Raphael et al., 2006), the risk of OCD was higher in those with fibromyalgia, compared to those without.

Clinic-based studies have been less consistent. Ghanizadeh et al. (2008) found higher rates of OCD in children with functional abdominal pain (n = 45) than in pain-free controls (n = 45). Conversely, the study by Atkinson et al. (1991) did not find significant differences in the prevalence of OCD between 97 cases of low-back pain and 49 matched controls. The rest of identified studies (Asmundson et al., 1996; Fishbain et al., 1986; Hocaoglu et al., 2008; Kinney et al., 1993; Mehraban et al., 2014; Polatin et al., 1993; Walker et al., 1997) lack control groups without pain symptoms and include relatively small sample sizes (n range=69–283), leading to a broad range of prevalence of OCD in these pain cohorts (range=0–61.3%).

Hence, while population-based studies seem to support an association between OCD and chronic pain, clinical studies (generally without control groups and likely to be subjected to biases) have shown mixed results. Larger studies with sufficient control of confounders are needed.

10. Mortality

A study of 15,440 individuals followed for up to 27 years from the Epidemiologic Catchment Area Program in the US (Eaton et al., 2013) reported that OCD (n = 388, of which 112 had died) was associated with a 22% reduced risk of death (HR=0.78, 95% CI 0.63–0.95). In contrast, a much larger Danish population-based study of 3270,650 individuals followed up a mean of 10 years (Meier et al., 2016) determined that the risk of mortality was double for those with OCD (n = 10,155, of which 110 had died), compared to the general population (mortality rate ratio=2.00, 95% CI 1.65–2.40). The risk of mortality remained largely unchanged when individuals with OCD were compared to their unaffected full siblings (mortality rate ratio=1.87, 95% CI 1.07–3.27). When analyzed separately, deaths due to both natural causes (including deaths by cancer, cardiac diseases, respiratory diseases, digestive conditions, deaths due to other somatic illness, and unknown causes) and unnatural causes (including homicides, accidents, and suicides) were both higher in individuals with OCD than in the controls. However, in both the American and the Danish studies (Eaton et al., 2013; Meier et al., 2016), the number of deceased individuals was too small to explore specific causes of death in further detail; thus, we know very little about specific natural causes of death in OCD.

In a large Swedish population-based study, Mataix-Cols et al. (2021) explored the risk of injuries or deaths due to transport accidents and motor vehicle accidents in individuals with OCD, compared to individuals from the general population and unexposed siblings. The authors concluded that the risks of serious transport accidents in OCD are negligible and heavily influenced by psychiatric comorbidity. These findings await replication but, if confirmed, they would indicate that traffic accidents are not a major specific cause of death in OCD, unlike in other disorders such as attention-deficit/hyperactivity disorder (Chang et al., 2017).

Two large population-based Swedish studies with long-term follow-ups have focused on deaths by suicide (Fernandez de la Cruz et al., 2017; Sidormchuk et al., 2021). These studies reported a markedly increased risk of deaths by suicide in OCD, compared to unaffected individuals, showing a 4- to 10-fold higher risk in OCD. These figures are significantly higher than those reported in older studies, which considered OCD a disorder of low risk for suicide (Coryell, 1981; Goodwin et al., 1969; Kringle, 1965). Moreover, Sidormchuk et al. (2021) found that both OCD and suicide deaths coaggregate in families, and that this is largely due to genetic factors. However, the contribution of unique environment was also significant. Attempts to identify risk factors are relevant to eventually reduce fatal outcomes in this patient group. In the population-based study by Fernandez de la Cruz et al. (2017), a previous suicide attempt was the variable that most increased the risk of subsequent suicide death. Other significant variables were a comorbid substance use disorder or a personality disorder. A recent systematic review showed that increased rates of suicide attempts were associated with increased severity in obsessions and increased rates of substance use disorders and depressive symptoms (Pellegrini et al., 2020). As a suicide prevention strategy, patients with OCD should be systematically screened for these and other potentially relevant risk factors.
11. Discussion

Our narrative review has highlighted important gaps in our understanding of the general health of individuals with OCD. Growing evidence supports a strong association between OCD and autoimmune diseases, circulatory system diseases, and mortality due to suicide. Preliminary evidence also suggests links between OCD and dementia, insomnia, respiratory diseases, gastrointestinal diseases, migraine, and chronic pain, as well as all-cause mortality. Conversely, the current evidence does not support a specific association between OCD and cancer or epilepsy, but such associations should not be ruled out until larger population-based studies are conducted. These results require extension and replication before the full picture emerges. Additionally, many of the existing studies are limited by small sample sizes, lack of control groups, and insufficient control of confounders, amongst other methodological shortcomings. Epidemiological studies using nationwide population-based registers have the potential to overcome some of these limitations and generate more accurate association estimates, but have been underused.

Understanding the mechanisms behind these associations may provide crucial information to guide the development of prevention and early intervention efforts. Presumably, the causes underlying the observed associations will likely be multifactorial and involve, among others, a combination of genetic factors shared between OCD and certain medical conditions, their interaction, and/or other causal factors, such as chronic medication use, unhealthy lifestyles or inequalities in the use of health services (Fig. 1).

OCD is moderately heritable (Mataix-Cols et al., 2013) and may share a genetic vulnerability with at least some of the reviewed medical outcomes (which are themselves heritable to various degrees). For example, we have shown that the association between OCD and suicidality is likely explained by a combination of common genetic liability and non-shared environmental effects (Krebs et al., 2021; Sidorchuk et al., 2021). This genetic correlation could be explained by the same set of genes being responsible for the liability to both OCD and certain health outcomes (i.e., pleiotropy). As the power of genome-wide association studies in OCD increases and reaches a “gene discovery zone” (Mahjani et al., 2021), it may be possible to design Mendelian randomization studies to explore whether OCD risk variants influence the appearance of certain medical conditions (Emdin et al., 2017; Wootton et al., 2021). Another possibility is that gene-environment correlations are relevant, where individuals with a genetic vulnerability for OCD would be more likely to engage in (similarly partly genetic) risk behaviors (e.g., sedentary lifestyle, alcohol use), which in turn are associated with adverse medical outcomes. In both the non-shared environmental and the gene-environment correlation scenarios, it should be possible to intervene to reduce, for example, cardiometabolic or suicidal risk. Another potential mechanism is gene by

Obsessive-compulsive disorder (OCD) may be associated with adverse health outcomes through a combination of pleiotropic genetic factors (rG) and other causal factors (i.e., environmental) via mediating environmental effects, which could partly be due to gene-environment correlations (rGE).

Fig. 1. Hypothesized causal mechanisms behind the associations between obsessive-compulsive disorder and adverse health outcomes.
environment interaction, whereby the nocice impact of environmental risk factors is influenced by the person’s genetic make up. For example, chronic medication use may only lead to metabolic disorders in genetically vulnerable individuals (Kao and Muller, 2013).

Some theories suggest that OCS themselves could contribute to adverse health-related outcomes. It has been hypothesized that contamination obsessions could lead to avoidance of medical consultations, preventing early detection and diagnosis of medical problems (Aguglia et al., 2018), and that washing and cleaning compulsions could lead to dermatological (Aguglia et al., 2018) and respiratory problems (Withhauer et al., 2014) that could in part be attributed to washing and cleaning compulsions through the increased exposure to chemicals in cleaning agents, which has been linked to some respiratory diseases (e.g., occupational asthma) (Carder et al., 2019; Medina-Ramon et al., 2005). These theories are speculative and remain to be formally tested.

The impact of chronic medication use, particularly antipsychotics, on the general health of patients with OCD has rarely been investigated, primarily due to the difficulty to design clinical trials with sufficiently long follow-up periods. The few observational studies that have focused on this topic have yielded inconclusive results (Albert et al., 2013; Chen et al., 2021; Isomura et al., 2018). Future research would benefit from the use of sophisticated pharmacopeidmiological and experimental designs to approach this critical question.

Another hypothesis is that the sometimes-severe loss of function inherent to the disorder could lead to unhealthy lifestyles (e.g., sedentary life, poor diet, alcohol and tobacco use), which would be particularly relevant for the development of cardiometabolic conditions and cancers. It is well documented that individuals with other psychiatric disorders (e.g., psychosis) have unhealthy lifestyles, which have in turn been linked with higher rates of morbidity and mortality in these conditions (Costa et al., 2018; Stubbs et al., 2016). Conversely, research on the lifestyles of individuals with OCD is very limited and should be prioritized. Albert et al. (2013) showed that individuals with OCD and metabolic syndrome were more likely to smoke and be physically inactive, compared to those with OCD without metabolic syndrome. In Aguglia et al. (2018), individuals with OCD with general medical conditions reported lower levels of physical activity, compared to individuals with OCD but no medical conditions. These results need replication in larger samples, focusing on a broader range of lifestyle habits. This knowledge will be essential for the design of lifestyle modification strategies aimed at reducing risk or preventing adverse health outcomes in OCD.

The known inequalities in the use and provision of healthcare services in individuals with psychiatric disorders is also worth considering. Individuals with psychiatric disorders are less likely to seek help for health-related issues and attend medical check-ups, and also less likely to receive health interventions and drug prescriptions, potentially leading to delays in the detection and treatment of diseases (Hippi-sley-Cox et al., 2007; Kisel y et al., 2013, 2016; Roberts et al., 2007). Aguglia et al. (2018) showed that individuals with OCD and comorbid medical conditions had a higher duration of untreated OCD, compared to those without medical issues. This may indicate that individuals whose OCD is better monitored from early on are in a better position to detect and treat their somatic comorbidities in a timely way. Importantly, inequalities in the use of services are particularly marked in ethnic minorities with OCD (Fernández de la Cruz et al., 2016, 2015).

Whether the above-described associations and potential pathways are specific to OCD or related to a general psychopathology dimension, the so-called p-factor (Caspi et al., 2014), is yet to be properly examined. Nonetheless, register-based studies including individuals with different psychiatric conditions assessed for their risk of subsequent medical conditions have shown that the magnitude of the risks varies across both psychiatric and medical conditions (Momen et al., 2020), justifying research into specific mental disorders. Furthermore, it would be wise to assume that interventions that effectively improve the general health of individuals with, say, schizophrenia will also work for individuals with OCD.

This review is not without limitations. Given the scarcity of literature on the topic, we chose to conduct a traditional narrative review as the most time-efficient way to identify gaps in the literature. However, these reviews can be considered subjective given that they rely on the authors’ previous knowledge and they generally do not present an exhaustive, unbiased or systematic summary (Munn et al., 2018). We hope that, as the knowledge in the area grows, more specific questions can be posed and addressed by methodologically sound systematic reviews and meta-analyses. Additionally, it should be born in mind that this review includes studies of differing methodological quality. This is an emerging field of study and the results gathered so far have to be expanded and replicated in different populations before they can be considered definitive.

To conclude, efforts should be made to improve access to services and engage individuals with OCD in treatment early on, providing them with broader health care that, ideally, also targets non-psychiatric and functional outcomes (Mataix-Cols et al., 2020). While OCD symptom reduction remains a priority, clinicians should also focus on monitoring the general health of persons with OCD and promoting healthy lifestyles.

Acknowledgements

This study is supported by grants from the Swedish Research Council for Health, Working Life and Welfare (FORTE), Sweden (grant number 2019-00438), Region Stockholm, Sweden (grant number 202000139), and Karolinska Institutet, Sweden (grant number 2020-01361), all awarded to Dr Fernández de la Cruz.

Disclosures

Dr Fernández de la Cruz receives royalties for contributing articles to UpToDate, Wolters Kluwer Health and for editorial work from Elsevier. Prof Mataix-Cols receives royalties for contributing articles to UpToDate, Wolters Kluwer Health. All other authors report no potential conflicts of interest.

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