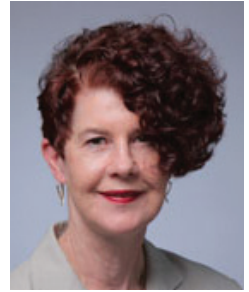


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**Many people with TS develop one or more co-morbidities. What is the time course of the most prevalent of these conditions? In particular, when do OCD, ADHD and/or depression typically first appear, how do they progress over time and do they recede or worsen during adulthood?**

Clinically referred youth with TS are often diagnosed with co-morbid psychiatric disorders, which typically emerge during childhood, although their timing and expression can be highly variable. ADHD and OCD are more likely than tics to persist into adulthood, and to be associated with more functional impairment and impact on quality of life. In general, adults with TS are more likely than children to present with obsessions and compulsions, mood disorders and a history of self-injurious behaviors.

Half or more of children with TS evaluated in clinical settings also meet criteria for Attention Deficit Hyperactivity Disorder (ADHD), with symptom onset usually preceding tic onset. ADHD symptoms are usually persistent, although past or current tics appear to have little impact on ADHD outcome. Learning disabilities and executive dysfunctions are generally reported to persist, although long-term outcomes are variable and complicated, with limited available data.

Obsessive-compulsive disorder (OCD) is diagnosed in approximately 20-40% of children who come to a clinic for TS; however, up to 90% may have some obsessive or compulsive symptoms. OC symptoms (OCS) may develop before, simultaneously with, or after onset of tics; OCS frequently emerge or intensify in early adolescence, while the impact of tics usually diminishes. Qualitative adult outcome of those with persistent OCB/OCS may be associated with social anxiety and poor self-esteem.

Much less is known about the onset and course of mood and non-OCD anxiety disorders in TS, although they also frequently co-occur. Generalized anxiety and mood disorders tend to persist, perhaps even in most adults with TD, and may impose a significant toll on functional outcome.

Overall, psychiatric comorbid disorder outcomes are generally thought to be semi-independent of tic outcomes. However, a recent study of older adolescents with TS reported that compared with healthy controls, individuals with TS had significantly higher rates of ADHD, learning disorder, conduct disorder and major depression. In the individuals with TS, poorer psychosocial outcomes were associated with greater ADHD, OCD and tic severity. Although much of the impairment was attributable to ADHD, this study was the first to report that individuals with TS were more likely to develop other psychiatric disorders (except OCD) and major depression, independent of ADHD.

**Some individuals with TS may develop depression and other co-morbidities that affect their social well-being. Are these co-morbidities a direct result of having to deal with underlying tics or are they independent entities?**

Studies have reported a greater lifetime risk for depression in individuals with TS, but data has largely been lacking on the nature and etiology of this association. Some authors have suggested the reason for this association is a possible genetic relationship between tics and depression, and others have conceptualized this association as a function of living with a chronic illness, which can be extremely stressful and debilitating. Others have suggested that there is likely to be a multifaceted interaction between lifetime stress and genetic vulnerabilities.

Some data have suggested that a complex interaction between tic severity, ADHD, OCD and psychosocial stress renders individuals with TS more likely to develop depression. However, the most recent study of older adolescents with TS reported that major depression was the only co-morbid disorder for which there was no association with a lifetime diagnosis of OCD, ADHD or any measure of ADHD, OCD or tic severity. This association remained robust after controlling for the presence of ADHD diagnosis and severity. This finding, which is the first to suggest a possible innate or biological link between TS and depression, raises some interesting new questions, and requires additional research.

**People with TS often have anxiety, ADD, ADHD and anger. Do these features result from distractions and excessive attention due to the presence of tics? Further, do these co-morbidities improve when tics decline spontaneously or in response to medication?**

Many studies have supported an association between clinically referred individuals with TS and psychiatric symptoms and/or disorders, such as anxiety, ADHD and explosive outbursts or rage attacks. In understanding the etiology of non-tic symptoms in individuals with TS, it is important to distinguish normal emotion from symptom from disorder. Anxiety and anger, for example, are within the spectrum of normal emotional response which can occur in all individuals, but may be experienced at higher rates or more intense levels in individuals with TS. Anxiety and anger, especially at higher levels, may also occur as symptoms of a variety of psychiatric disorders, such as OCD, separation anxiety disorder, oppositional defiant disorder or a mood disorder. Symptoms of hyperactivity, reduced concentration, distractibility and/or impulsivity, which impact academic, interpersonal or occupational functioning, are the core features of ADHD, and may often co-occur with anxiety, anger and poor frustration tolerance.

Although the presence of tics in an individual with TS may result in temporarily reduced concentration, or emotional reactions of anxiety or anger, tics do not necessarily cause these features, since there are alternative explanations for their etiology. It is often the case that anxiety, anger and reduced concentration resulting directly from tics can be attenuated with effective treatment of the tics themselves. However, if the anxiety, anger or reduced concentration are symptoms of an anxiety or mood disorder or ADHD, then tic treatment alone is not usually enough to reduce these symptoms. Interestingly but not surprisingly, treatment of some co-morbid symptoms or disorders, such as anxiety, may also secondarily reduce the tics. More research is needed to disentangle many of these symptoms and features. □