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Pre- and perinatal complications in relation to Tourette syndrome and co-occurring obsessive-compulsive disorder and attention-deficit/ hyperactivity disorder



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ABSTRACT

Pre- and perinatal complications have been implicated in the onset and clinical expression of Tourette syndrome albeit with considerable inconsistencies across studies. Also, little is known about their role in co-occurring obsessive-compulsive disorder (OCD) and attention-deficit/hyperactivity disorder (ADHD) in individuals with a tic disorder. Therefore, we aimed to investigate the role of pre- and perinatal complications in relation to the presence and symptom severity of chronic tic disorder and co-occurring OCD and ADHD using data of 1113 participants from the Tourette International Collaborative Genetics study. This study included 586 participants with a chronic tic disorder and 527 unaffected family controls. We controlled for age and sex differences by creating propensity score matched subsamples for both case-control and within-case analyses. We found that premature birth (OR = 1.72) and morning sickness requiring medical attention (OR = 2.57) were associated with the presence of a chronic tic disorder. Also, the total number of pre- and perinatal complications was higher in those with a tic disorder (OR = 1.07). Furthermore, neonatal complications were related to the presence (OR = 1.46) and severity (b = 2.27) of co-occurring OCD and also to ADHD severity (b = 1.09). Delivery complications were only related to co-occurring OCD (OR = 1.49). We conclude that early exposure to adverse situations during pregnancy is related to the presence of chronic tic disorders. Exposure at a later stage, at birth or during the first weeks of life, appears to be associated with co-occurring OCD and ADHD.

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1. Introduction

Chronic tic disorders are childhood-onset neuropsychiatric disorders characterized by the presence of multiple motor tics and/ or one or more vocal tics persisting for at least one year (American Psychiatric Association, 2000). Tourette syndrome (TS) is the best studied chronic tic disorder. While family and twin studies have consistently indicated a genetic etiology for tic disorders, environmental factors are also involved (Mataix-Cols et al., 2015; Price et al., 1985). Pre- and perinatal complications are particularly important environmental factors associated with many neuropsychiatric disorders (Tomasović et al., 2012) and have also been implicated in tic disorders (Chao et al., 2014; Hoekstra et al., 2013). Pioneering work by Pasamanick and Kawi reported that mothers of children with tics experienced pre- and perinatal complications 1.5 times more often compared to mothers of children without tics (Pasamanick and Kawi, 1956).

Although there has been a steady, albeit slow, increase in the number of studies investigating pre- and perinatal complications in association with TS (see Chao et al., 2014 for a recent review), findings across studies have been remarkably inconsistent. This makes it difficult to draw valid conclusions with regard to the role of pre- and perinatal factors (7). For example, maternal smoking during pregnancy was associated with TS in some studies (Cubo et al., 2014; Mathews et al., 2006), but not in others (e.g., Bos-Veneman et al., 2010; Mathews et al., 2014; Motlagh et al., 2010). Another example is younger maternal age, that was identified as a factor for TS in one study (Khalifa and von Knorring, 2005), whereas other studies reported no association (Burd et al., 1999; Motlagh et al., 2010). This emphasizes the need for additional studies.

Study design limitations and use of small sample sizes most

likely contributed to these inconsistent findings. That is, most epidemiological studies of general population samples typically lacked clinician-confirmed diagnosis of a tic disorder and/or included relatively few affected individuals (e.g., Atladóttir et al., 2007; Mathews et al., 2014), whereas clinical samples may have been biased by over-representation of more severe cases (Leckman et al., 1990; Saccomani et al., 2005). Finally, possible confounding variables, such as socio-economic status (SES), parity, and parental age, have not always been taken into account (Bos-Veneman et al., 2010; Mathews et al., 2006; Pringsheim et al., 2009).

Another largely unresolved issue, due to the scarcity of studies, is the role of pre- and perinatal factors in relation to the expression of the disease, i.e., tic symptom severity and the presence and/or severity of co-occurring conditions (Chao et al., 2014). Preliminary evidence has indicated maternal smoking as a possible risk factor not only for the diagnosis of a tic disorder but also severity of tics (Bos-Veneman et al., 2010; Mathews et al., 2006). Two of the most frequent co-occurring conditions are attention-deficit/hyperactivity disorder (ADHD; present in 40-60% of cases, Roessner et al., 2007) and obsessive-compulsive disorder (OCD; present in 30-50% of cases, Wanderer et al., 2012). In co-occurring OCD, older paternal age (Mathews et al., 2006) and forceps delivery (Santangelo, 1994) have been implicated, whereas low birth weight, premature birth, and maternal smoking were associated with co-occurring ADHD (Leivonen et al., 2015a; Pringsheim et al., 2009), but these findings have not been replicated (Chao et al., 2014).

The aim of the present study was to investigate the role of a broad set of pre- and perinatal complications in relation to diagnosis and symptom severity of TS and other chronic tic disorders, and to the presence and severity of co-occurring OCD and ADHD within the Tourette International Collaborative Genetics (TIC

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