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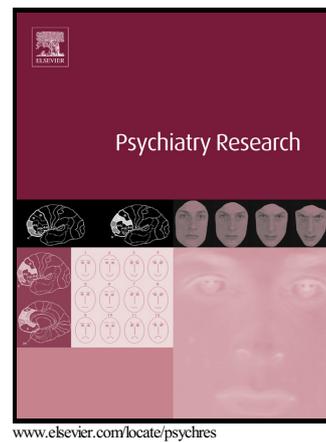
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Interpersonal Reactivity Differences in Tourette Syndrome

Clare M. Eddy^{a,b}, Antonella Macerollo^c, Davide Martino^{d,e} & Andrea E. Cavanna^{a,b,c,f}

^a Birmingham and Solihull Mental Health NHS Foundation Trust, Department of Neuropsychiatry, The Barberry National Centre for Mental Health, Birmingham, UK

^b School of Clinical and Experimental Medicine, College of Medical and Dental Sciences, University of Birmingham, Birmingham, UK

^c Sobell Department of Motor Neuroscience and Movement Disorders, National Hospital of Neurology and Neurosurgery, Institute of Neurology and University College London, London, UK

^d Department of Neurology, King's College Hospital NHS Foundation Trust, London, UK

^e Queen Elizabeth Hospital, Woolwich, Lewisham & Greenwich NHS Trust, London, UK

^f School of Life and Health Sciences, Aston University, Birmingham, UK

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Correspondence to: Dr Clare M. Eddy, Department of Neuropsychiatry, The Barberry, 25 Vincent Drive, Edgbaston, Birmingham, UK, B15 2FG, Tel: 0121 301 2514 Fax: 0121 301 2291

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ABSTRACT

Tourette syndrome (TS) frequently involves complex tics with social significance, including imitation or socially inappropriate behaviours. This study explored everyday perspective taking and empathic tendencies in ninety-five patients with TS and sixty healthy controls. Analyses indicated that both males and females with TS exhibited a different interpersonal reactivity profile to controls, characterised by a reduced tendency to take other people's perspectives, and elevated personal distress in response to intense emotional situations (e.g. people experiencing crises).

Emotion; social cognition; Tourette syndrome

1. INTRODUCTION

In Tourette syndrome (TS), motor and vocal tics are frequently accompanied by complex tics with social relevance, including imitation (echophenomena), and socially inappropriate behaviours (Kurlan et al., 1996; Eddy and Cavanna, 2013a,b). Patients' symptoms can interfere with social interaction and relationships (Wadman et al., 2013), and negatively impact quality of life (Eddy and Cavanna, 2013a,b). Furthermore, TS may be associated with differences in reasoning about the mental states of others (Eddy et al., 2010a; Eddy et al. 2010b; Eddy et al., 2011; Channon et al., 2012). The study of social cognition may therefore help unravel the neuropsychological mechanisms contributing to patients' symptoms.

The Interpersonal Reactivity Index (IRI: Davis, 1980) assesses empathy and individual perspective taking tendencies. Interpersonal reactivity has been explored in many clinical conditions, and can be altered in schizophrenia (Lehmann et al.,

2014), obsessive-compulsive disorder (Fontenelle et al., 2009), depression (Cusi et al., 2011) and the movement disorder Huntington's disease (Eddy et al., 2014).

Importantly, studies have shown that interpersonal reactivity can be related to impulsivity (Beven et al., 2004) and everyday social functioning capacity (Abramowitz et al., 2014).

In this study we used the IRI to test the hypothesis that TS is characterised by differences in the tendency to adopt alternative perspectives and to relate emotionally to others in everyday life. We also assessed relationships between interpersonal reactivity and patients' symptoms. Measures of the severity of tic symptoms and mood disorder were used, in addition to scales for the commonly co-morbid conditions obsessive-compulsive disorder (OCD) and attention deficit hyperactivity disorder (ADHD).

2. METHODS

2.1 Subjects

The study was approved by the local NHS research ethics committee and all volunteers provided written informed consent. The IRI was completed by 95 adults with TS according to DSMV criteria (30 females, 65 males) and 60 healthy controls (30 females, 30 males) recruited through BSMHFT and University of Birmingham. Patient co-morbidities included OCD (6 females, 11 males) ADHD (1 female, 13 males), and OCD+ADHD (2 females, 3 males). Fifty-eight patients (42 males, 16 females) were taking medications (atypical antipsychotics=35; SSRIs=24;

clonidine=17; typical antipsychotics=8; combination=19). Patients with TS completed scales assessing tics, OCD, ADHD, anxiety and depression.

2.2 Assessment

2.2.3 *Interpersonal Reactivity Index (IRI)*

The IRI (Davis, 1980) contains 28 items responded to using a 5-point Likert scale deciding how well the statement sounds like themselves (e.g. “Does not describe me well”=0 to “Describes me very well”=4). There are four subscales containing 7 items: Perspective Taking (PT: tendencies towards taking the perspective of others); Fantasy (the predisposition to transpose the self and imagine others’ experiences through stories); Empathic Concern, (EC: reactions of sympathy and concern towards other people in difficult circumstances); Personal Distress (PD: tendencies towards stress or anxiety in relation to intense interpersonal interactions). Subscale scores range from 0-28.

2.2.4 *Yale Global Tic Severity Scale (YGTSS)*

This clinician rated scale (Leckman et al., 1989) assesses overall tic severity. Motor and vocal tics are scored in terms of tic number, frequency, complexity, intensity and interference.

2.2.5 *Premonitory Urge for Tics Scale (PUTS)*

The PUTS (Woods et al., 2005) includes 9 items assessing the sensory and mental phenomena linked the premonitory urges which frequently precede tics. The higher the score the greater frequency/intensity of premonitory urges.

2.2.6 Obsessive Compulsive Inventory-Revised (OCI-R)

OCD symptoms can be assessed using this 18-item, self-report, 5-point likert scale (Foa et al., 2002). Higher scores indicate more severe symptoms.

2.2.7 Adult ADHD Self-Report Scale (ASRS)

The current study used a subset of six questions from the original ADHD scale, which have been shown to outperform the full scale in diagnosing ADHD in adults (Kessler et al., 2005).

2.2.8 Hospital Anxiety and Depression Scale (HADS)

This scale (Zigmond and Snaith, 1983) consists of 7 items to assess depression, and seven to measure anxiety. Analysis used totals for each subscale.

2.3 Statistical analyses

To control for gender, patient and control group comparisons were conducted separately for males and females. Further within-group analyses in TS explored whether any clinical symptoms correlated with the IRI sub-scale scores. IRI subscale mean scores showed different variances for patients and controls so non-parametric Mann-Whitney U (MWU) tests were applied.

3. RESULTS

There were no significant age differences for the groups (males: MWU=985, $p=0.936$; females: MWU=442, $p=0.906$).

IRI subscale scores are shown in Table 1. Male patients with TS exhibited significantly lower scores to male controls for PT (MWU=1,526, $p<0.001$), and significantly higher scores for PD (MWU=624.5, $p=0.005$). This pattern was also apparent for females with TS in comparison to female controls (PT: MWU=612.5, $p=0.016$; PD: MWU=225.5, $p=0.001$). No other between-group differences were found (males, fantasy: MWU=1,147, $p=0.168$; males, EC: MWU=1,025, $p=0.673$; females, fantasy: MWU=442.5, $p=0.909$; females, EC: MWU=558, $p=0.109$). Four between-group comparisons were made for males, and four for females. With an adjusted significance threshold of $0.05/8=0.006$, three of the four findings would remain significant. However, this correction is likely to be too strict, as testing males and females separately led to lower power, and applying non-parametric tests can also lead to a greater risk of type II error.

Correlations were conducted for the whole patient group between tics and premonitory urges, OCD, ADHD, anxiety, or depression and the IRI subscales (PT and PD) for which patients differed to controls. Two correlations were significant at $<.05$ but wouldn't survive correction for multiple comparisons ($0.05/12=0.004$). PD scores were positively related to ADHD ($Sr=0.224$, $p=0.030$), and negatively related to tic severity ($Sr=-0.282$, $p=0.006$).

4. DISCUSSION

Individuals with TS exhibited a different IRI profile to healthy age and gender-matched controls, comprising of a reduced tendency to take other people's perspectives, and elevated personal distress when faced with other people in emotional crises. The same pattern was apparent for both males and females, despite evidence that gender differences may influence IRI scores (Paro et al., 2014).

Previous studies have found that patients with TS can exhibit differences in social and emotional reasoning (Eddy and Cavanna, 2013c). The current findings provide further evidence that TS is associated with changes in social cognition as reflected in self-reported everyday behaviour. Changes in interpersonal reactivity may also be related to other psychosocial aspects of TS, including differences in personality (Balottin et al., 2009; Eddy et al., 2013) and attachment styles (Dehning et al., 2014).

These findings are similar to those reported for other clinical groups. For example, Fujino et al (2014) reported reduced PT and increased PD in schizophrenia, and PD scores were negatively correlated with fractional anisotropy in the splenium of the corpus callosum. The PT subscale is thought to measure cognitive empathy, while the PD subscale is a measure of emotional empathy (Davis, 1983). Our findings therefore indicate differences in both cognitive and affective empathy in TS. It is interesting to note that lower PT scores can be associated with impulsivity (Beven et al., 2004), and impulsive behaviours are common in TS (e.g. Wright et al., 2012).

The items assessing PD relate to uncomfortable or overwhelming emotional reactions in emergencies or other social situations when other people are in distress. Elevated PD in TS could be mediated by increased emotional dysregulation or

anxiety in social situations. Taking this finding together with the lower PT scores may suggest that problems with controlling emotional reactions towards other people may contribute to people with TS being less inclined to adopt other peoples' perspectives. For example, reduced PT could constitute an avoidance or compensation strategy, to help preserve emotional stability. Similar explanations have been applied in other clinical populations. For example, elevated PD can precede the onset of reduced cognitive empathy in psychosis (Achim et al., 2011).

Increased PD in TS may be suggestive of greater emotional contagion. It is already thought that these patients exhibit enhanced motor contagion, due to the frequency of echoing tics. In addition, one study exploring the influence of observed movements on executed actions in TS revealed evidence of motor interference when these patients observed biological movements that were incompatible with their own movements (Jonas et al., 2010). A recent insightful review of the pathophysiology of echophenomena suggested that such findings may reflect dysfunctional prefrontal control over motor and/or mirror neuron system activations (Ganos et al., 2012). Future studies should determine whether echoing tics and emotional contagion are associated with increased PD in TS.

Previous clinical studies have found that scores on the IRI, including PD scores, can be associated with anxiety or depression (e.g. Fontenelle et al., 2009; Abramowitz et al., 2014). Such relationships were not apparent in the current study. As we did not observe a correlation between anxiety ratings and increased PD, this supports the interpretation that PD is a separate construct from more generalised anxiety, constituting a more specific response during intense emotional situations.

A negative relationship was found between tic severity and PD ratings. As increased personal distress may indicate poorer emotional regulation, this indicates

that emotion regulation is inversely related to tics. A simple interpretation would be that having more severe tics may mean that patients with TS are frequently exposed to uncomfortable social situations so could learn to become less emotionally sensitive to unpleasant emotional experiences. However, the TS group as a whole exhibited significantly greater PD than healthy controls. Perhaps a more parsimonious explanation is that while individuals with TS are more likely to experience problems with emotion regulation (i.e. higher PD ratings than people without tics), expressing tics more frequently may actually help with this, perhaps by relieving inner tension. Mediating factors could further explain this relationship. For example, a greater need for suppression techniques in patients with more frequent tics may make these individuals better equipped at dealing with emotion control in stressful situations. Alternatively, patients with more frequent tics may be more likely to use medication, which may help with emotional reactivity.

As most patients were medicated, this is a key limitation of the study. A further limitation is that the sample of patients was from a single specialist outpatient clinic. The study would have been strengthened by the inclusion of additional measures of social cognition and IQ. Nonetheless, we can conclude that TS is associated with alterations in interpersonal reactivity. Further work is needed to determine whether these alterations in social cognition reflect neurobiological changes or the psychosocial effects of having tics.

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Table 1. Interpersonal Reactivity Index scores and age for the patient and control groups

Group		Fantasy		Perspective taking		Personal Distress		Empathic Concern		Age	
		Mean, SD	Median, range	Mean, SD	Median, range	Mean, SD	Median, range	Mean, SD	Median, range	Mean, SD	Median, range
Patients with Tourette syndrome	Females (n=30)	15.45, 7.65	16.00, 0-28	15.20, 7.27	14.00, 3-28	17.43, 4.98	17.00, 8-29	19.97, 4.62	20.50, 10-27	32.17, 13.30	29.00, 17-58
	Males (n=65)	13.83, 6.51	13.00, 0-27	12.74, 5.48	12.00, 4-25	15.28, 5.69	16.00, 1-28	19.05, 4-11	19.00, 9-28	29.85, 14.57	25.00, 17-64
Healthy controls	Females (n=30)	15.67, 4.81	16.00, 5-24	19.40, 4.51	20.00, 10-27	12.20, 5.39	12.50, 2-19	21.73, 4.26	23.00, 8-28	33.03, 16.48	22.50, 17-61
	Males (n=30)	15.43, 5.33	17.00, 5-24	18.00, 4.00	18.00, 9-26	12.00, 5.51	11.50, 3-27	19.60, 4.26	19.50, 12-28	31.43, 14.90	26.00, 18-65

Highlights

- Tourette syndrome is associated with a reduction in everyday perspective taking
- Patients also show elevated distress during intense emotional situations

- These differences may reflect emotional dysregulation and compensatory strategies
- Altered interpersonal reactivity can help explain differences on theory of mind tasks

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