Psychoneuroendocrinology (2014) 44, 30—34

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevier.com/locate/psyneuen

SHORT COMMUNICATION

Cortical thickness correlates of socioemotional difficulties in adults with Turner syndrome

Jean-François Lepage [a,*], **Cédric Clouchoux** [b], **Maryse Lassonde** [a,c], **Alan C. Evans** [b], **Cheri L. Deal** [c], **Hugo Théoret** [a,c]

[a] *Département de psychologie, Université de Montréal, Canada*
[b] *Montréal Neurological Institute, McGill University, Montréal, Canada*
[c] *Centre de Recherche du Centre Hospitalier Universitaire Sainte-Justine, Montréal, Canada*

Received 12 December 2013; received in revised form 14 February 2014; accepted 24 February 2014

KEYWORDS
Emotional Quotient Inventory;
Social cognition;
Turner syndrome;
X-monosomy;
Sex-chromosome aneuploidy

Summary Turner syndrome (TS) is a non-inherited genetic disorder associated with a specific cognitive phenotype and socioemotional impairments. The present study aimed at characterizing the neuroanatomical basis of socioemotional dysfunctions in TS using the Emotional Quotient inventory (EQ-I) and cortical morphology analysis in 17 individuals with TS (45,X) and 17-age and verbal IQ matched healthy females. Individuals with TS reported significantly greater socio-emotional impairment than controls. Cortical thickness analysis showed that participants with TS had an overall thicker cortex than controls, with extensive alterations in the temporal, frontal, parietal and insular regions bilaterally. Using the total EQ-I score as regressor in the cortical thickness analysis revealed a number of brain regions where the relationship between cortical thickness and EQ-I score differed between groups; these areas included brain regions critically involved in socioemotional processes, such as bilateral insula, the anterior cingulate and the orbitofrontal cortex. These results show that socioemotional dysfunctions seen in women with TS are associated with significant alterations in brain morphology.

* Corresponding author at: Spaulding Rehabilitation Hospital, Massachusetts General Hospital, 79-96 13th St. Charlestown, MA 02129, USA. Tel.: +1 819 387 6997.
E-mail address: jf.lepage@gmail.com (J.-F. Lepage).

http://dx.doi.org/10.1016/j.psyneuen.2014.02.017
0306-4530/

1. Introduction

Turner syndrome (TS) is caused by the absence of one X-chromosome in females. In addition to motor deficits, visuospatial and executive dysfunctions, individuals with TS often present social and emotional problems (Burnett et al., 2010). Indeed, women with the disorder often show increased shyness, social anxiety, low self-esteem (Ross et al., 2000; Schmidt et al., 2006), and a higher risk of depression (Cardoso et al., 2004). This increased vulnerability to affective and social disorders, combined with impairments at tasks probing social cognition (Lawrence et al., 2003), strongly suggests alterations of the neurocognitive network involved in socio-emotional functioning and regulation.

Recent neuroimaging studies conducted in TS have revealed the existence of substantial structural alterations in multiple brain regions, with several involving social and emotional processing. These modifications include enlarged amygdala (Lepage et al., 2013a), but also aberrant cortical thickness in areas such as the superior temporal sulcus, insula, fusiform, orbitofrontal and anterior cingulate cortex (Raznahan et al., 2010; Lepage et al., 2013a). While these cerebral modifications provide a plausible neural basis for the social and emotional impairments in TS, establishing the precise neural network associated with socioemotional deficits in TS would help understand the role of the X-chromosome in social cognition as well as provide insight into its contribution to sex-biased psychopathologies bearing important affective and social components. Here, we used the Bar-On Emotional Intelligence Quotient, a well-established measure of socioemotional abilities, in conjunction with cortical thickness analysis to delineate the cortical correlates of socioemotional difficulties in adults with TS.

2. Materials and methods

2.1. Participants

Subjects were recruited through the endocrinology clinic of the CHU-Sainte-Justine. Participants with TS were considered eligible to take part in the study if they were healthy and presented a complete X-chromosome monosomy (45,X) as demonstrated by peripheral blood karyotypes with no normal cell lines, mosaicism or Y chromosome material and an analysis of buccal epidelium DNA consistent with a 45,X karyotype. Seventeen participants with TS met these criteria (all Caucasians, right handed; mean age: 24.51 ± 4.93; 11 with an X-chromosome from maternal origin, six from paternal origin). Hormone replacement status and clinical severity score of all TS subjects was obtained through medical files. All were being cycled on oral contraceptives because of gonadal failure. Seventeen sex and age-matched healthy controls were also recruited (all Caucasians, right handed; mean age: 26.90 ± 6.78). All patients were euthyroid at the time of testing, as evidenced by normal TSH values, and all were scheduled during days 7—14 of their menstrual cycle ($N = 6$ controls) or days 7—10 of oral contraceptive use (all participants with TS and 11 controls). Written informed consent was obtained from all participants and the experimental protocol was approved by the *Comité d'éthique de la recherche du CHU-Sainte-Justine* and was in accordance with the Declaration of Helsinki. Women in the current study also participated in previously published work (Lepage et al., 2013b).

2.2. Genetics

Leukocyte and buccal epithelial DNA was extracted from duplicate peripheral blood samples drawn from the participants and their mothers. PCR conditions were optimized for 14 highly polymorphic X chromosome microsatellites chosen after their high degree of heterozygosity (mean = 78%) and their allele frequencies ($\leq$47%). Amplification of most microsatellites was achieved with commercially available primers (MapPairs Human Markers) through Invritogen Corp. The Genome DataBase web site (http://www.gdb.org) was used to obtain allele number and size specifications. X^{intact} genotype parental origin was determined with comparisons between mothers and their daughters for different combinations of microsatellites depending on the daughter's karyotype.

2.3. Neuropsychology

The neuropsychological assessment was conducted in a single session by a certified neuropsychologist. The Wechsler Abbreviate Scale of Intelligence was used to measure verbal, performance and full-scale IQ. Participants also filled-out the Bar-On Emotional Quotient Inventory (EQ-I; Bar-On, 1997), a self-administered scale made of 133 items using a five-point Likert scale that taps social and emotional strengths and weaknesses. The test gives a global emotional quotient (EQ-I Total score), which sums up the scores obtained on five principal composite scales assessing major aspects of social functioning and personal monitoring: (1) intrapersonal; (2) interpersonal; (3) stress management; (4) adaptability; and (5) general mood. The EQ-I has been shown to be a valid measure of emotional intelligence and to correlate well with other instruments that measure related concepts (Bar-On, 1997).

2.4. Cortical thickness

A Siemens Sonata 1.5 T was use to acquire T1-weighted magnetic resonance imaging (MRI) sequences for all subjects with to the following acquisition parameters: three-dimensional fast-field echo scan with 160 slices, 1 mm isotropic resolution, repetition time of 18 ms, echo time of 10 ms, flip angle of 30°. The Montreal Neurological Institute cortical thickness pipeline was used to process data for all subjects. Each T1-weighted image volume was corrected for signal intensity non-uniformity and linearly transformed into standard MNI-space (ICBM152 template). An automatic tissue classification algorithm then classified the transformed images into gray matter, white matter, and cerebrospinal fluid. The white and gray matter surfaces were then fitted using deformable spherical mesh models, resulting in two surfaces with 81,920 vertices each. Cortical thickness can be defined as the distance between linked vertices since each vertex (or point) on the white matter surface is related to its gray matter surface counterpart. Cortical thickness was measured at every vertex and blurred using a 30 mm surface-based kernel.