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Alexithymia, Emotion Perception, and Social Assertiveness in Adult Women with Noonan and Turner Syndromes

Renée L. Roelofs,[1,2,3,4]* Ellen Wingbermühle,[1,3] Kim Freriks,[5] Chris M. Verhaak,[6] Roy P. C. Kessels,[2,3,6] and Jos I. M. Egger[1,3,4]

[1]Centre of Excellence for Neuropsychiatry, Vincent van Gogh Institute for Psychiatry, Venray, the Netherlands

[2]Centre of Excellence for Korsakoff and Alcohol-Related Cognitive Disorders, Vincent van Gogh Institute for Psychiatry, Venray, the Netherlands

[3]Donders Institute for Brain, Cognition and Behaviour, Radboud University Nijmegen, Nijmegen, the Netherlands

[4]Behavioural Science Institute, Radboud University Nijmegen, Nijmegen, the Netherlands

[5]Division of Endocrinology, Department of Internal Medicine, Radboud University Medical Center, Nijmegen, the Netherlands

[6]Department of Medical Psychology, Radboud University Medical Center, Nijmegen, the Netherlands

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Noonan syndrome (NS) and Turner syndrome (TS) are associated with cognitive problems and difficulties in affective information processing. While both phenotypes include short stature, facial dysmorphisms, and a webbed neck, genetic etiology and neuropsychological phenotype differ significantly. The present study examines putative differences in affective information processing and social assertiveness between adult women with NS and TS. Twenty-six women with NS, 40 women with TS, and 40 female controls were matched on age and intelligence, and subsequently compared on (1) alexithymia, measured by the Bermond-Vorst Alexithymia Questionnaire, (2) emotion perception, evaluated by the Emotion Recognition Task, and (3) social assertiveness and social discomfort, assessed by the Scale for Interpersonal Behavior. Women with TS showed higher levels of alexithymia than women with NS and controls (P-values < 0.001), whereas women with NS had more trouble recognizing angry facial expressions in comparison with controls ($P = 0.01$). No significant group differences were found for the frequency of social assertiveness and the level of social discomfort. Women with NS and TS demonstrated different patterns of impairment in affective information processing, in terms of alexithymia and emotion perception. The present findings suggest neuropsychological phenotyping to be helpful for the diagnosis of specific cognitive-affective deficits in genetic syndromes, for the enhancement of genetic counseling, and for the development of personalized treatment plans.

Key words: Noonan syndrome; Turner syndrome; affective information processing; alexithymia; emotions; emotion perception; cognition; social assertiveness; contextual neuropsychology; psychopathology

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INTRODUCTION

In 1938, Henry Turner described females with sexual infantilism, a webbed neck, and short stature. Two decades later, many women with these characteristics appeared to have a partial or complete aneuploidy of the second X chromosome, which was named Turner syndrome (TS) [Sybert and McCauley, 2004]. Later, males and females with normal sex chromosomes were identified who showed phenotypical resemblances to TS. This led to confusing and incorrect terms such as "male TS," "female pseudo-Turner," or "XX and XY Turner phenotype" [Collins and Turner, 1973]. Noonan and Ehmke [1963] recognized this disorder, now known as Noonan syndrome (NS), to be essentially different from TS in terms of genetic etiology. NS is caused by germline mutations in the

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*Correspondence to:
R.L. Roelofs, Centre of Excellence for Neuropsychiatry, Vincent van Gogh Institute for Psychiatry, Stationsweg 46, 5803 AC Venray, the Netherlands.
E-mail: rroelofs@vvgi.nl

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Ras/mitogen-activated protein kinase (Ras-MAPK) pathway, a signal transduction cascade involved in several developmental processes [Tartaglia et al., 2011]. Although the genotypes differ, the phenotypes of NS and TS are quite similar, sharing several physical features, such as short stature, facial anomalies, a webbed neck, skeletal malformations, and cardiac problems [Elsheikh et al., 2002].

Cognitive functioning in adults with NS has recently been studied by Wingbermühle et al. [2012a]. In comparison with matched healthy controls, they found a lowered speed of information processing in individuals with NS, but no impairments in other cognitive domains. Intelligence scores were slightly lower in comparison with the average population. In contrast, a review concerning cognitive functioning in NS suggested a more diffuse pattern of cognitive problems in children and adolescents [Wingbermühle et al., 2009]. Intelligence levels in the low-average range were reported, with verbal and performance capacities fairly evenly distributed. In addition, group studies in children with NS found impairments in one or several of the following areas: language skills, motor functioning, working memory and memorizing, selective or sustained attention, and organizational and planning capacities [Wingbermühle et al., 2009; Pierpont et al., 2013]. Thus, children with NS seem to display more diffuse cognitive deficits compared to adults, but longitudinal studies have not yet been performed to confirm this.

Studies on cognitive deficits are more numerous in individuals with TS than in NS and typically report a low-average to average full-scale intelligence, with (nearly) normal levels of verbal intelligence, and a lower performance intelligence [Nijhuis-van der et al., 2003]. Impaired visuospatial information processing is considered the hallmark cognitive deficit in TS, but difficulties in executive functioning, (visual) memory, perceptual organization, math processing, motor abilities, specific aspects of language (e.g., verbal fluency), attention deficits, and hyperactivity have been reported frequently [Elsheikh et al., 2002; Nijhuis-van der et al., 2003; Rovet, 2004; Hong et al., 2009; Knickmeyer, 2012]. Planning skills seem to improve with age, while visuospatial and visual memory deficits remain in adulthood [Romans et al., 1997].

Besides cognitive impairments, both NS and TS have been associated with problems in affective information processing, notably social cognition [Burnett et al., 2010; Wingbermühle et al., 2012b], that is, constructing representations of the relations between oneself and others, and to use those representations flexibly to guide social behavior [Adolphs, 2001]. Studies addressing social cognition in children with NS are mainly limited to single-case studies and report below-average social skills, diminished social insight, and social immaturity [Troyer and Joschko, 1997; Sarimski, 2000; Lee et al., 2005]. Adviento et al. [2013] found a higher prevalence of social impairment in children and adults with RASopathies in comparison with sibling controls. In adults with NS, difficulties in identifying and describing feelings (i.e., alexithymia), slight overall problems in the perception of emotional facial expressions, and social discomfort (but no avoidance of social situations) have been described [Wingbermühle et al., 2012b]. TS has been associated with social immaturity, problems in social relations, difficulties in expressing emotions, social anxiety, and impairments in facial emotion recognition, most notably fear [Burnett et al., 2010; Hong et al., 2014]. Despite similarities in phenotypic presentation between women with NS and TS, it should be noted that within the groups heterogeneity in cognitive and social-emotional problems is present.

Impairments in social cognition are associated with psychological distress, social isolation, and reduced self-esteem [Beauchamp and Anderson, 2010]. Moreover, alexithymia is known to constitute a risk factor for developing mood and anxiety problems [Larsen et al., 2003]. Studies mention the presence of mood and anxiety problems in individuals with NS [Mahendran and Aw, 1989; Verhoeven et al., 2004; Noonan, 2005; Verhoeven et al., 2008; Wingbermühle et al., 2009; Alfieri et al., 2014]. However, besides studies reporting autism traits and ADHD symptoms in individuals with NS in comparison with siblings [Adviento et al., 2013; Pierpont et al., 2014], to our knowledge, no controlled studies have been performed concerning psychopathology in NS. Depressive problems and anxiety have been reported in individuals with TS in addition to lowered levels of self-esteem [Downey et al., 1989; Delooz et al., 1993; Kilic et al., 2005; Saad et al., 2014]. Other studies, in contrast, mention that the frequency of emotional problems in individuals with TS is not higher than in comparable populations [Ross et al., 2000; Cardoso et al., 2004; Schmidt et al., 2006].

The aim of the current study was to compare alexithymia, emotion perception, and social assertiveness of females with NS with that of females with TS and female controls. This may lead to the discrimination of specific profiles of affective information processing in NS and TS, which could contribute to the development of tailored clinical approaches. We hypothesized that (1) women with TS show lower levels of alexithymia than women with NS, specifically less problems in verbalizing emotions due to their relatively higher verbal skills, whereas women with NS will show higher levels of alexithymia than controls; (2) women with TS perform worse on facial emotion perception (especially for recognizing fear) than both women with NS and controls, women with NS show a slightly lower overall emotion perception performance in comparison with controls; and (3) women with TS and women with NS will show more social discomfort than controls because of their deviant physical appearance. A deviant appearance, deviant behavior, deviant characteristics, and disabilities were identified as causes of childhood bullying [Thornberg, 2010]. Many individuals with NS have been bullied in childhood (76.92% in the current sample). Bullying victims are at risk for developing mood and anxiety disorders, and show problems in social relationships [Takizawa et al., 2014]. Women with TS will display more avoidance in social situations than controls, women with NS show equal levels of avoidance in comparison with controls.

MATERIALS AND METHODS

Participants

Twenty-six females with NS, 40 females with TS, and 40 female controls participated in this study. All participants took part in larger on-going investigations [Menke et al., 2010; Wingbermühle et al., 2012a; Wingbermühle et al., 2012b; Freriks et al., 2013; Freriks et al., 2015]. Participation was voluntary and written informed consent was obtained from all participants or their legal representatives. The study was approved by the Institutional Review Board of the Vincent van Gogh Institute for Psychiatry and by the

Committee on Research involving Human Subjects Arnhem/Nijmegen of the Radboud University Medical Center, in accordance with the Declaration of Helsinki. Women with NS were consecutively referred to the Vincent van Gogh Institute for Psychiatry by the Department of Human Genetics of the Radboud University Medical Center. Inclusion criteria were a confirmed clinical diagnosis of NS and a minimum age of 16 years. Women with TS were recruited by the Department of Medical Psychology of the Radboud University Medical Center. They were included if they had a karyotype result consistent with TS and a chronological age of 16 years or more. For the distribution of the karyotypes and molecular test results, see Table I. A female control group of adult community-dwelling volunteers was recruited via the network of the researchers involved in the data collection. Exclusion criteria for the controls were a (known) diagnosis of a genetic or neurological disorder or a current psychiatric illness.

In view of the controversy regarding the contribution of intelligence to social emotional constructs such as alexithymia [Taylor et al., 1988; Parker et al., 1989; Parker et al., 2001; Ibanez et al., 2013], women with TS and controls were carefully matched to the group of women with NS on age and full scale IQ on the Wechsler Adult Intelligence Scale (WAIS-III), supported by statistical between-group testing of these variables. Full-scale IQ (FSIQ), verbal IQ (VIQ), and performance IQ (PIQ) were estimated with an abbreviated version of the WAIS-III, derived from the seven-subtest short form of Ward [Ward, 1990]. The present short form included eight subtests: four verbal subtests (Information, Digit Span, Arithmetic, and Similarities), and four performance subtests (Picture Completion, Picture Arrangement, Block Design, and Digit Symbol). The seven-subtest short form of Ward is known to generate reliable estimates of FSIQ, as well as satisfactory estimates of VIQ and PIQ [Pilgrim et al., 1999; Axelrod et al., 2000; Axelrod et al., 2001]. The sum of the scaled sores of the verbal subtests was multiplied by 1.5 and the sum of the performance subtests was multiplied by 1.25 in order to obtain the estimated VIQ, PIQ, and FSIQ [Wechsler, 2005].

Descriptive information of the groups is presented in Table II. As a result of the matching process, no significant group differences were found on age ($F(2,103) = 1.01$, $P = 0.37$) and WAIS-III FSIQ ($F(2,103) = 0.05$, $P = 0.95$). There were significant group effects for VIQ ($F(2,103) = 3.14$, $P = 0.05$) and PIQ ($F(2,103) = 7.25$, $P = 0.001$), but Bonferroni post-hoc analyses failed to reach significance for VIQ ($P = 0.07$). Post-hoc tests showed that PIQ of women with TS was lower than that of women with NS ($P = 0.002$) and controls ($P = 0.01$). Within the groups, we found VIQ to be higher than PIQ in the TS group ($t(39) = 6.42$, $P < 0.001$) and PIQ higher than VIQ in the NS group ($t(25) = -2.23$, $P = 0.04$). No significant difference was found between VIQ and PIQ in the control group. Education level was coded according to the Verhage system, ranging from category 1 (1–5 years of education) to 7 (19–20 years of education) [Bouma et al., 2012]. Education levels differed significantly between the three groups ($H(2) = 23.15$, $P < 0.001$). Follow-up tests indicated that, despite their equal full scale intelligence levels, women with TS were better educated than women with NS ($P < 0.001$) and controls ($P = 0.001$).

Since anxiety and mood problems are known to impede affective information processing [Bourke et al., 2010; Plana et al., 2014], we included the anxiety and depression scales of the Dutch version of the Symptom Checklist-90 Revised (SCL-90-R) [Arrindell and Ettema, 2003] for control purposes. Women with NS (N = 25) reported significantly higher levels of anxiety ($F(1,63) = 7.52$, $P = 0.01$, $\eta^2_p = 0.11$) and depression than women with TS ($F(1,63) = 6.77$, $P = 0.01$, $\eta^2_p = .10$).

TABLE I. Distribution of the Karyotypes of Women With Noonan and Turner Syndromes

Karyotype	Number (%)
Noonan syndrome (N = 26)	
PTPN11	14 (53.85)
SOS1	4 (15.38)
KRAS	1 (3.85)
No mutation found	2 (7.69)
Unknown	5 (19.23)
Turner syndrome (N = 40)	
45,X	17 (42.5)
45,X/46,XX	5 (12.5)
45,X/47,XXX	2 (5)
45,X/46,Xi(Xq)	5 (12.5)
45,X/46,X,del(X)	2 (5)
45,X/46,XX/47,XXX	1 (2.5)
45,X/46,X,r(X)	2 (5)
46,X,i(Xq)	4 (10)
46,X,del(X)	1 (2.5)
46,X,Xp-/46,X,i(Xq) [10/6]	1 (2.5)

Alexithymia

To assess alexithymia, the Bermond-Vorst Alexithymia Questionnaire (BVAQ) [Vorst and Bermond, 2001] was administered. The BVAQ is a self-report questionnaire designed to measure five factor based dimensions of alexithymia: *(1) Emotionalizing* (the degree to which someone is emotionally aroused by emotion inducing events); *(2) Fantasizing* (the degree to which someone is inclined to fantasize, imagine, and daydream about virtual matters), *(3) Identifying* (the degree to which one is able to define the nature of one's own emotions);*(4) Analyzing* (the degree to which one seeks explanations of one's own emotional reactions); and *(5) Verbalizing* (the degree to which one is able or inclined to describe or communicate about one's emotional reactions). The subscales *Emotionalizing* and *Fantasizing* together constitute the higher order *Affective Component* and the subscales *Identifying, Analyzing,* and *Verbalizing* compose the higher order *Cognitive Component*. The BVAQ consists of 40 items (e.g., "when something totally unexpected happens, I remain calm and unmoved" or "when I am distressed, I know whether I am afraid or sad or angry"), which are rated on a five-point Likert scale ranging from 1 to 5. Each of the five dimensions is measured by eight items. The scores on the subscales range from 8 to 40 and the total alexithymia score ranges from 40 to 200. Higher scores are indicative of higher levels of alexithymia [Vorst and Bermond, 2001].

TABLE II. Descriptive Information of Women With Turner Syndrome, Noonan Syndrome, and Controls

	Turner syndrome (N = 40)			Noonan syndrome (N = 26)*			Controls (N = 40)		
	M/mode	Range	SD	M/mode	Range	SD	M/mode	Range	SD
Age	25.44	19–33	3.27	27.85	16–52	12.05	28.28	17–52	11.46
WAIS-III FSIQ	90.68	75–106	9.30	91.42	71–119	11.82	91.05	75–106	6.97
VIQ	96.25	75–116	9.97	90.35	67–121	12.85	92.00	74–108	8.04
PIQ	86.00	67–106	10.39	94.77	74–113	11.97	92.45	78–113	7.86
Education level	6	4–6	–	5	2–7	–	5	3–7	–
SCL-90-R									
Anxiety	13.08	10–27	3.75	16.60	7–35	6.62	–	–	–
Depression	22.93	16–46	7.83	29.52	16–59	12.65	–	–	–

Note: M, mean; SD, standard deviation; WAIS-III, Wechsler Adult Intelligence Scale Third Edition; FSIQ, full scale intelligence quotient (estimated by eight subtests); VIQ/PIQ, estimated verbal/performance intelligence quotient; SCL-90-R, Dutch version of the Symptom Checklist-90 Revised.
*The sample size for the SCL-90-R analyses was 25.

Emotion Perception

The Emotion Recognition Task (ERT), developed by Montagne et al. [2007], is a computer-generated paradigm for the recognition of six basic facial emotional expressions: anger, disgust, fear, happiness, sadness, and surprise. Participants are presented with dynamic images of the faces of four actors (two males and two females) expressing the aforementioned emotions in different intensities. A computer program enables real-time interactive morphing between neutral expression and the facial expression of diverse emotional intensities, presented as video clips [Montagne et al., 2007; Kessels et al., 2014]. After each video clip, the participant is asked to make a forced choice between the six emotions, displayed in labels on the test computer. The emotion recognition scores of women with NS, women with TS, and controls were compared on the intensities 40, 60, 80, and 100%. Performance was defined by the number of correctly labeled emotional expressions. For each emotion, scores may range from 0 to 16. Higher scores represent better emotion perception.

Social Assertiveness and Social Discomfort

The Scale for Interpersonal Behavior (SIB) was used as an index for the engagement in social behavior and the amount of discomfort evoked by these situations [Arrindell et al., 2001]. The SIB includes 50 items (e.g., "start a conversation with a stranger" or "tell someone that you like him/her"), which the participant has to evaluate on two separate five-point scales; one for the probability of engagement in specific social situations (performance) and one for the amount of discomfort experienced in these situations (distress). Besides a total performance and total distress score, the SIB results in four factorially based subscales: *(1) Display of negative feelings*; *(2) Expression of and dealing with personal limitations*; *(3) Initiating assertiveness*; and *(4) Praising others and the ability to deal with compliments/praise of others* [Arrindell et al., 2001]. For this study, the total performance score and total distress score were calculated.

Statistical Analysis

A multivariate analysis of variance (MANOVA) was performed to compare the results on the BVAQ and SIB of women with NS, TS, and controls. BVAQ and SIB scores were included as dependent variables, and Group (NS, TS, C) was included as a factor. The ERT was analyzed with a mixed between-within subjects ANOVA, with Emotion (Fear, Happiness, Sadness, Surprise, Disgust, Anger) and Intensity (40, 60, 80, 100) as within-subject factors, and Group (NS, TS, C) as between-subject factor. This analysis was followed up by six mixed between-within subjects ANOVAs, one for each of the emotions, with Intensity (40, 60, 80, 100) as within-subject factor and Group (NS, TS, C) as between-subject factor, to investigate the influence of group on emotion perception scores for the six emotions separately. Effect sizes were computed, expressed as partial eta-squared. All analyses have been performed with SPSS 22 for Windows.

RESULTS

Alexithymia

Significant group differences were found on the total BVAQ score, the Affective Component, the Cognitive Component, and on the dimensions Identifying, Emotionalizing, and Analyzing. All *F*-values were larger than 9.80 (*P*-values < 0.001, η_p^2 ranged between 0.16 and 0.35). Bonferroni post-hoc analyses revealed that women with TS reported more alexithymic features than both women with NS and controls, and that women with NS did not differ from controls with respect to alexithymia levels, with exception of the scale Emotionalizing. Women with NS showed lower levels of alexithymia on this scale than controls. An overview of the BVAQ results is displayed in Table III.

Social Assertiveness and Social Discomfort

No significant group differences were found for the reports on the performance scale and distress scale of the SIB. An overview of the results is displayed in Table III.

TABLE III. Mean Scores and Standard Deviations of the BVAQ and SIB Variables for Women With Turner Syndrome, Noonan Syndrome, and Controls

		Turner syndrome (N = 40)	Noonan syndrome (N = 26)	Controls (N = 40)	Post-hoc tests
Alexithymia	BVAQ Total score	137.78 (12.82)	104.77 (18.89)	116.25 (24.33)	TS vs. NS**/TS vs. C**
	Affective component	51.93 (8.78)	41.62 (9.92)	46.75 (9.47)	TS vs. NS**/TS vs. C*
	Fantasizing	23.65 (6.93)	23.15 (6.34)	24.87 (6.82)	–
	Emotionalizing	28.28 (4.21)	18.46 (5.04)	21.87 (6.75)	TS vs. NS**/TS vs. C**/NS vs. C*
	Cognitive component	85.85 (11.55)	63.15 (13.05)	69.50 (19.52)	TS vs. NS**/TS vs. C**
	Verbalizing	25.03 (5.58)	24.88 (5.90)	23.73 (6.94)	–
	Identifying	30.55 (5.33)	18.69 (7.07)	22.85 (8.62)	TS vs. NS**/TS vs. C**
	Analyzing	30.28 (4.64)	19.58 (4.67)	22.92 (7.96)	TS vs. NS**/TS vs. C**
Social Assertiveness & Social Discomfort	Scale of Interpersonal Behavior				
	Performance score	154.40 (25.89)	142.96 (34.28)	155.85 (33.91)	–
	Distress score	116.38 (33.77)	120.19 (47.90)	101.30 (26.34)	–

Note: BVAQ, Bermond-Vorst Alexithymia Questionnaire; SIB, Scale for Interpersonal Behavior; TS, Turner syndrome; NS, Noonan syndrome, C, Controls.
$^{*}P < 0.05$, $^{**}P < 0.001$, all *P*-values are Bonferroni corrected.

Emotion Perception

Mauchly's test indicated that the assumption of sphericity had been violated for the main effect of Emotion ($\chi^2(14) = 35.54$, $P = 0.001$) and for the interaction effect of Emotion and Intensity ($\chi^2(119) = 286.19$, $P < 0.001$). Therefore, the degrees of freedom were corrected using Greenhouse-Geisser estimates of sphericity. The mixed between-within subjects ANOVA revealed no significant effect of Group, indicating that the three groups did not significantly differ in accuracy of emotion perception. Significant main effects were found for Emotion ($F(4.50, 463.67) = 187.23$, $P < 0.001$, $\eta_p^2 = 0.65$) and Intensity ($F(3, 309) = 85.09$, $P < 0.001$, $\eta_p^2 = 0.45$), indicating that some emotions were more difficult to recognize than others and that performance varied between the different levels of emotion intensity. A small interaction effect was found for Emotion and Intensity ($F(11.26, 1159.86) = 4.77$, $P < 0.001$, $\eta_p^2 = 0.04$), indicating that intensity did not affect the recognition of each emotion in the same way, which is in accordance with previous findings [Montagne et al., 2007]. Moreover, there was a small interaction effect of Emotion and Group ($F(9.00, 463.67) = 2.10$. $P = 0.02$, $\eta_p^2 = 0.04$), but the interaction effect of Intensity and Group, and the three-way interaction between Emotion, Intensity, and Group were not significant.

To further examine the significant interaction effect of Emotion and Group, six mixed between-within subjects ANOVAs were performed, one for each emotion. These analyses showed a significant group effect only for the emotion anger ($F(2, 103) = 5.44$, $P = 0.01$, $\eta_p^2 = 0.10$). Bonferroni post-hoc comparisons indicated that women with NS were less accurate in recognizing anger than controls ($P = 0.005$). For a graphical display of the ERT results, see Figure 1.

DISCUSSION

This first comparative study of affective information processing in women with NS, TS, and female controls, showed differential patterns of impairment for women with NS and women with TS. Women with TS demonstrated higher levels of alexithymia than women with NS and controls, whereas women with NS only showed problems in recognizing angry facial expressions in comparison with controls.

Surprisingly, women with TS reported higher levels of alexithymia than women with NS and controls. They particularly reported lower emotional arousal, more difficulties in defining the nature of their emotions, and more problems in seeking explanations for emotional reactions. No significant group differences were found in the ability to verbalize emotional experiences or in the ability to fantasize. The pattern of reported alexithymic problems in women with TS is indicative of "affective" alexithymia (as opposed to the "cognitive" variant), in which problems in the awareness of the arousal of emotions are thought to hamper the interpretation of emotions [Vorst and Bermond, 2001]. Although it was hypothesized that women with TS would specifically show fewer problems in verbalizing emotions, finding substantially higher levels of general alexithymia was unexpected. Considering earlier reports of higher levels of cognitive alexithymia in men and women with NS in comparison with controls [Wingbermühle et al., 2012b], we expected that these findings would be replicated in the current study. However, the present sample of women with NS did not report more alexithymic traits than controls or women with TS. A meta-analysis on sex differences in alexithymia [Levant et al., 2009] concluded that higher levels of alexithymia are present in men, especially in those with a traditionally masculine gender-role socialization. Consequently, males with NS may report higher

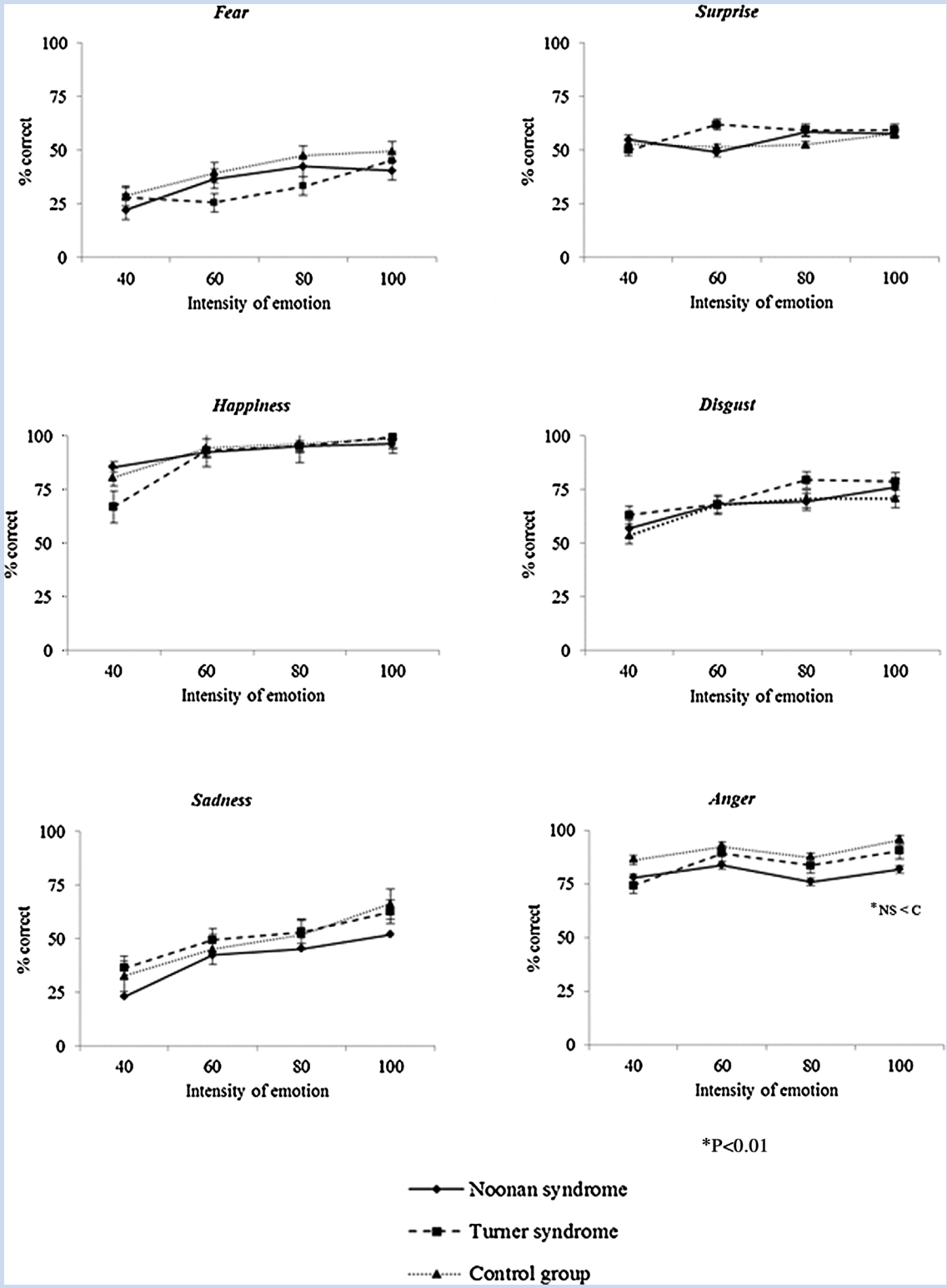

FIG. 1. Percentage of correctly recognized facial emotional expressions on the Emotion Recognition Task, for the different levels of intensity (40–100%) of the six emotions. Results were displayed for 26 women with Noonan syndrome (NS), 40 women with Turner syndrome (TS), and 40 controls (C). Error bars represent the standard error of the mean.

levels of alexithymia than females with NS, which could explain why the previously mentioned effects in a mixed-sex sample were not replicated in the current study.

Moreover, women with NS demonstrated specific difficulty in recognizing angry facial expressions in comparison with controls; the accuracy of the recognition of other emotional expressions was at control level. This is not in accordance with the findings in a previous study of our research group, in which individuals with NS showed a lower emotion recognition score in general, but no specific emotion perception problems [Wingbermühle et al., 2012b]. Mood and anxiety problems are known to impede affective information processing. Our sample of women with NS reported higher levels of depression and anxiety on the SCL-90-R than women with TS, which could have led to a response bias toward negative stimuli. However, this is less likely to affect the response to angry facial expressions in isolation. In order to investigate the relation between depression and anxiety symptoms on the SCL-90-R and emotion recognition on the ERT in women with NS, Pearson correlation coefficients were calculated. Only a significantly positive correlation between reported depression and the total ERT score was found ($r(23) = .42$, $P = 0.04$). The correlations between depression and anxiety scores, and the mean anger recognition score did not reach significance (anxiety $r(23) = -0.13$, $P = 0.53$; depression $r(23) = .19$, $P = 0.36$). This is in contrast with our suggestion that higher levels of depression and anxiety could explain the poor recognition of angry faces in women with NS. In fact, these results indicate that women with NS who reported more depressive symptoms were more accurate in recognizing facial emotions. However, the meaning and relevance of the specific anger recognition impairment in women with NS remains unclear and requires replication. In contrast to our hypothesis, women with TS did not demonstrate the frequently reported deficit in fear recognition [Romans et al., 1997; Lawrence et al., 2003a; 2003b; Mazzola et al., 2006; Skuse et al., 2005; Hong et al., 2014]. These studies used facial emotional expressions of fixed intensities to measure affect recognition. However, the ERT we used presented moving images of facial expressions of different emotional intensities. Perhaps, women with TS benefitted from the presentation of fearful faces in the lower intensities, explaining why their performance on the recognition of fearful faces is higher in the current study than in previous reports.

Women with NS, women with TS and controls reported equal levels of distress in social situations and described comparable frequencies of engaging in these situations on the SIB. Despite the lack of group differences on the total performance and total distress scores, we found that women with NS experienced more distress than controls while initiating assertiveness ($P = 0.01$), and that they were less likely to express and deal with personal limitations ($P = 0.01$) in comparison with women with TS. This could indicate a tendency toward a socially anxious behavior style in women with NS. This is in accordance with the results of a previous study of Wingbermühle et al. [2012b], reporting that individuals with NS experienced more social discomfort than controls, but did not avoid social interaction.

A major strength of this study is that it represents the first systematic investigation comparing affective information processing between women with NS, women with TS, and female controls. Other strengths are the inclusion of sizeable same-sex groups, matched on age and intelligence. However, education levels differed between the groups, as women with TS were able to complete higher levels of education than both other groups. The lag in education level of the NS group is in line with previous studies, which demonstrated a higher need of special education in individuals with NS compared to IQ-matched controls, possibly due to additional cognitive difficulties [Shaw et al., 2007; Wingbermühle et al., 2012a]. In turn, TS women may benefit from their relative verbal strength during education. A second limitation of this study concerns the fact that the outcome measures were confined to the visual perception of emotional expressions and to self-reports of alexithymia and social assertiveness. These constructs are important elements of affective information processing, but affective functioning is a much more broader domain. Including more diverse measures to investigate other aspects of affective information processing would be desirable (e.g., perspective taking, auditory emotion perception, or real-life social interaction). However, in the present study design, neurocognitive testing already lasted approximately 8 hr (spread over two consecutive days); a more extensive examination would not have been feasible in this sample.

In conclusion, affective information processing was examined in two phenotypically comparable, but genetically different syndromes, showing different patterns of affective information processing. While women with TS showed higher levels of alexithymia, women with NS only showed specific impairments in anger recognition. Since alexithymia has not previously been described in TS, this is a novel and interesting finding. The presence of dissimilar patterns of affective information processing in NS and TS groups suggests that the difference in genetic etiology contributes to the specific social cognitive profiles, rather than the social consequences of having a deviant physical appearance. Imaging studies in TS describe an increased volume of the amygdala, an area of the brain associated with affective information processing [Kesler et al., 2004], while in NS, mutations in the Ras-MAPK pathway are suggested to result in abnormal brain development and functioning without a specific neural structure known to be affected yet [Wingbermühle et al., 2012a]. Since affective information processing is required for adequate daily functioning and greatly influences quality of life [Beauchamp and Anderson, 2010], this cognitive-affective domain should be an area of consideration within the treatment options of these syndromes. Both individuals with NS and TS could benefit from treatment focusing on the improvement of affective information processing, in which alexithymia or emotion perception should be accentuated depending on the specific impairments of the individual.

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