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RESEARCH ARTICLE

Social attention as a cross-cultural transdiagnostic neurodevelopmental risk marker

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Abstract

The primary objectives of this study were to evaluate the structure and age-related stability of social attention in English and Arabic-speaking youth and to compare social attention between children with autism spectrum disorder (ASD), other developmental disabilities (DD), and typically-developing controls. Eye-tracking data were collected from US (N = 270) and Qatari (N = 242) youth ages 1–17, including children evaluated for possible ASD. Participants viewed 44 stimuli from seven social paradigms. Fixation was computed for areas of interest within each stimulus. Latent variable models examined the structure of social attention. Generalized estimating equation models examined the effect of age, sex, culture, and diagnostic group on social attention. The best-fitting model included a general social attention factor and six specific factors. Cultural differences in social attention were minimal and social attention was stable across age ($r = 0.03$), but females showed significantly greater social attention than males ($d = 0.28$). Social attention was weaker in DD ($d = -0.17$) and lowest in ASD ($d = -0.38$) relative to controls. Differences were of sufficient magnitude across areas-of-interest to reliably differentiate DD from controls (AUC = 0.80) and ASD-only from all other cases (AUC = 0.76). A social attention dimension that represents an early-life preference for socially salient information was identified. This preference was cross-culturally consistent and stable across development but stronger in females and weaker in DD, especially ASD. Given rapid and easy-to-collect remote eye tracking administration, social attention measurement may be useful for developmental monitoring. Acquisition of population norms, analogous to height/weight/head circumference, might enhance early screening and tracking of neurodevelopment.

Lay Summary: This research found that social attention is a single dimension of behavior that represents a strong preference for social stimuli, is consistent across cultures, stable across age, and stronger in females. Children with developmental disabilities had lower levels of social attention than neurotypical children and children with autism spectrum disorder had the lowest levels of social attention.

KEYWORDS

autism, cross-cultural, developmental disability, risk marker, social attention, validation

INTRODUCTION

Social processes are basic functional dimensions that span the full range of behavior from neurotypical to disordered and are featured prominently in the National Institute of Mental Health Research Domain Criteria (RDoC) (Morris et al., 2015; Morris & Cuthbert, 2012). A key task of future research is to identify and improve the measurement of early emerging neurocognitive domains and to characterize how these domains impact typical and atypical development. One promising domain that has been suggested to play a key role across normative and atypical development is social attention (Frank et al., 2012; Salley & Colombo, 2016). However, several questions regarding its structure, measurement, and influence across different forms of developmental psychopathology remain. Specifically, it will be important to identify and differentiate the structure of social attention and understand how it relates to RDoC social processes and psychopathology.

More than 100 studies have examined the role of social attention in autism spectrum disorder (ASD), finding reductions in gaze to high social salience (hereafter social) information and increases in gaze to low social salience (hereafter non-social) information (Chita-Tegmark, 2016; Frazier et al., 2017). More specifically, meta-analytic studies have identified reduced attention to whole and upper face regions (Chita-Tegmark, 1996; Frazier et al., 2017; Papagiannopoulou et al., 2014), increased attention to body regions and other irrelevant or extraneous aspects of stimuli (Chita-Tegmark, 1996; Frazier et al., 2017), and variable but generally reduced attention to lower face (mouth) (Chita-Tegmark, 1996; Frazier et al., 2017). It has been suggested that reductions in social motivation underlie this observed pattern of gaze differences (Chevallier et al., 2012), although higher-order social cognitive deficits may also play a role for some gaze differences (Itier & Batty, 2009). Gaze findings can also be dependent on the type of stimuli or paradigm implemented. For example, attention to mouth regions likely reflects the content of the stimuli, with people with ASD showing greater reductions in gaze during speech perception conditions (Grossman et al., 2015; Irwin & Brancazio, 2014). While there do not appear to be substantial differences in gaze to static versus dynamic stimuli (Chita-Tegmark, 2016; Frazier et al., 2017), there has been conflicting evidence whether naturalistic or ecological stimuli (Chevallier et al., 2015; Chita-Tegmark, 2016). Similarly, there is debate as to whether gaze during live interactions produce different patterns of findings (Noris et al., 2012) or whether screen-based versus live interactions evaluate different aspects of social attention (Grossman et al., 2019).

Infant and toddler studies have identified that the above described alterations in social attention begin very early in life (Jones & Klin, 2013), and appear to be under strong genetic control in ASD and, more generally, during neurodevelopment (Constantino et al., 2017).

Together, these data suggest that individual variation in social attention may be a key building block of social development and an early indicator of atypical developmental trajectories, potentially informing RDoC domains. However, no studies have comprehensively evaluated the latent structure of social attention (Salley & Colombo, 2016), a key pre-condition to understanding its place within the RDoC framework and essential for developing useful measures for research and clinical practice.

Given that social attention is a complex construct, with many distinct paradigms used to elicit and measure individual differences, it is important to understand whether different paradigms are completely independent, and need to be mapped separately, or if one latent dimension saturates indicators across paradigms. A general social attention dimension, akin to general intelligence (Warne & Burningham, 2019), common executive function (Friedman & Miyake, 2017), or general psychopathology (Caspi et al., 2014), could provide a useful clinical summary, regardless of the specific measurement paradigms implemented. Furthermore, it is also important to clarify whether reductions in social attention are specific to ASD or might represent a transdiagnostic marker for abnormal neurodevelopment. While some data suggest specificity (N. Sasson et al., 2007), it is uncertain whether, and to what degree, social attention alterations may be present in children with other developmental disabilities (DD). If a broad reduction is observed in ASD and, to a lesser extent, in DD, social attention may be a useful marker for neurodevelopmental screening and building predictive outcome models, as well as for aiding clinical ASD diagnosis. Finally, the falling cost and ease of implementing remote eye-tracking measures of social attention suggests that these may be useful objective measurements for widespread adoption across the globe, but variance due to age, sex, and culture must first be understood.

Thus, the present study was motivated by limited data on how social attention processes aggregate, develop, or are influenced by other factors. The primary aim was to understand the structure of social attention. Secondary aims were to examine whether social attention processes are cross-culturally consistent, to explore their development across childhood, estimate sex differences, and identify differences in ASD and related DD. Using an Arabic culture provided large differences in collectivism versus individualism (Arabic culture tends to be higher on collectivism than the US, with a greater emphasis on family and loyalty), power distance (with Arabic culture again tending to be higher, with increased emphasis on cues of dominance and less social mobility across layers of interpersonal hierarchies), and interpersonal proxemics (with Arabic cultures tending to have less physical distance between people during social interactions) (Han et al., 2013; Hofstede & Bond, 1984; Minkov & Hofstede, 2011). In an infant/toddler sample, a recent study, using variance decomposition methods, identified

a content-independent factor measuring attention to social information (Chawarska et al., 2016). Therefore, our hypothesis was that a general social attention domain would emerge representing a preference for high social salience information. Specific factors representing attention to various types of high and low social salience information were also expected based on prior gaze studies, including attention to upper (Jones et al., 2008), lower (Tenenbaum et al., 2013), and whole face (Rogers et al., 2018) regions within stimuli. In spite of substantial cultural differences between US and Arabic culture, social attention preference was expected to be consistent across cultures, reflecting an early-acquired cognitive process (orienting to socially salient information) that is not substantially influenced by cultural factors. Furthermore, based on prior research examining gaze differences across age (Frazier et al., 2016; Frazier et al., 2018), sex (Frazier et al., 2016; Frazier et al., 2018; Harrop et al., 2019), and diagnostic groups (Chita-Tegmark, 1996, 2016; Frazier et al., 2017; Papagiannopoulou et al., 2014), social attention preference was expected to be relatively stable, stronger in females, and show a pattern of mild impairment in DD and greater impairment in ASD.

METHODS

Participants

US and Qatar samples consisted of (a) youth referred to multi-disciplinary ASD evaluation clinics and (b) typically-developing (hereafter neurotypical) controls (NT) recruited from local primary care clinics, unaffected siblings of clinic patients, or from researcher contacts. In the US sample, participants were recruited from May 15, 2015, to November 30, 2016. In the Qatar sample, after translating English-language stimuli into Arabic, participants were recruited from February 04, 2019, to March 14, 2020. Healthy control participants had no evidence of any developmental disability or neuropsychiatric condition as reported by parents/caregivers. Gaze data were collected by research personnel blinded to diagnosis. Clinical personnel were not privy to the results of gaze data collection. The Cleveland Clinic and Qatar Biomedical Research Institute IRBs reviewed and approved the research protocols. Additional methodological details are presented in Supplemental Methods. This study followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guidelines for case-control studies (Table S1).

Diagnosis

Consensus diagnosis was based on a parent interview and psychosocial history conducted by a psychologist,

medical evaluation and developmental history confirmed by a physician, and the Autism Diagnostic Observation Schedule-Second Edition (ADOS-2) completed by a reliable administrator. Within 2 weeks of the initial visit, a multidisciplinary team met to confirm the presence/absence of ASD using DSM-5 criteria and document other psychiatric diagnoses. Eligibility for participation in the DD group required any other neurodevelopmental or neuropsychiatric disorder diagnosis besides ASD. Eligibility in the NT group required no past or current developmental or psychiatric difficulties.

Clinical assessments

The ADOS-2 considered the gold-standard clinical observation measures for assessing autism symptom severity was used (Lord et al., 2012; Luyster et al., 2009). The ADOS-2 was administered to all referred cases in the US sample but only to confirm clinical ASD diagnosis or rule out possible ASD in the Qatar sample. The SRS-2 measured parent-reported autism trait levels (Constantino & Gruber, 2012). The SRS-2 is a 65-item, quantitative assessment of autism traits. The SRS sex-adjusted total T-score has been extensively validated and distinguishes youth with autism from other psychiatric conditions (Constantino & Gruber, 2005; Virkud et al., 2009). In the Qatar sample, SRS-2 total T-scores were estimated using the Arabic translated Social Communication Questionnaire total raw scores (Aldosari et al., 2019; Rutter et al., 2003), since these two measures have previously been shown to be highly correlated in large national samples with ASD and non-ASD participants ($n = 6700$, $r = 0.87$) (Frazier et al., 2012).

Eye-tracking acquisition and processing

Eye-tracking data were collected in a quiet room adjacent to the diagnostic clinic. Data were recorded using an SMI Red250 remote eye tracker (sampling at 60 Hz) attached to the frame of a 1280 × 1024 19-inch LCD stimulus presentation monitor. Maximum spatial resolution was 0.1° and maximum gaze position accuracy was 0.5°. The system allows for head movement (32 × 21 × 30 for Red250) at a maximum distance of 75 cm. Two 5-point calibrations were obtained at fixed times throughout the experiment. Fixation time percent (FTP) to each area-of-interest (AOI) were derived using SMI BeGaze software (SensoMotoric Instruments Inc., 2013). Fixation time percent is calculated by dividing the total fixation duration by the total possible time of the stimulus or AOI.

Forty-four stimuli were presented using SMI Experiment Center, selected to represent seven distinct stimulus paradigms previously used in the eye gaze literature (Frazier et al., 2017), including: single-person facial affect, two-person facial affect discrimination, gaze

following and joint attention, single speaker toward the participant, side-by-side abstract shapes and social scenes, pictures of people intermixed with autism restricted interest images, and naturalistic social interaction scenes. All but the two-person facial affect discrimination and pictorial stimuli were dynamic videos and three of the seven paradigms including people interacting. Each US stimulus was carefully reproduced to be culturally-appropriate for a Qatar population, (Figure S1a–h and Supplemental Methods). Both sets of stimuli were presented in the same order.

Within all stimuli, AOIs were designated across the entire stimulus duration and represented the following content: (1) upper face, (2) lower face, (3) whole face, (4) images of people scattered among images of autism-associated restricted interests, (5) body regions, (6) abstract shapes, (7) gestures, (8) relevant objects, and (9) irrelevant objects. These content areas and the associated AOIs were identified by the investigator based on prior research, including meta-analyses reporting on content Areas 1–3, 5, and 9 (Chita-Tegmark, 1996; Frazier et al., 2017; Papagiannopoulou et al., 2014), passive viewing preference studies reporting AOIs for content Areas 4 (Sasson et al., 2008) and 6 (Pierce et al., 2011; Shi et al., 2015), and research evaluating joint attention/directed gaze for content Areas 7–8 (Falck-Ytter et al., 2012; Frazier et al., 2016; Frazier et al., 2018). AOIs from each of these content areas were identified within each stimulus and averaged across stimuli within each paradigm. This resulted in 34 total AOI indicators across all nine content types. Only 21 AOI indicators from the first six content types were included in factor analyses because the remaining three content areas had AOI indicators with low average FTP across participants and very low communality estimates from exploratory factor analyses in the training sample. However, all 34 original AOI indicators were included in support vector machine analyses used to evaluate screening and diagnostic validity as low FTP and communality values are not relevant to these analyses.

Eye-tracking data collection followed recommendations from Sasson and Elison (Sasson & Elison, 2012). Children were seated alone or in their parent's lap ~65 cm from the LCD display and viewed stimuli subtending a visual angle of ~18.8°. Standard room lighting was used and the room was sparse, with visual barriers to reduce distraction. After calibration, children who were of sufficient age and cognitive level were told, "You will see some pictures and videos; pay attention, but look however you want." The total eye-tracking session was 6 min and 8 s long. Eye-tracking evaluations were considered invalid and data were excluded if gaze to the screen during the entire experiment was tracked <40% of the time, if more than two unplanned re-calibrations had to be inserted, or participants had <15 stimuli with adequate looking time (defined as ≥50% FTP).

Statistical analyses

Univariate and bivariate distributions did not identify any outliers or high leverage cases. Descriptive statistics are presented separately for US and Qatar samples. Independent samples *t* tests and Chi-square statistics were used to examine possible sample differences. Missing data were minimal (3.9% of all AOI indicators). Analyses tolerant of missing data were used where possible and, in other cases, five multiple imputation data sets were created and analyzed (Little & Rubin, 2002; Schafer & Graham, 2002). Results were highly consistent between original data and all imputations and therefore only results for the first imputation are presented.

To determine the latent structure of social attention indicators, the combined US and Qatar samples were split into training ($n = 256$) and testing ($n = 256$) subsamples. In the training sample, exploratory factor models from 1 to 6 factors were estimated to examine indicator communalities, identify plausible factor numbers, and determine the content distinctions of possible factors. Results of these analyses suggested 4–6 factors as plausible. The content types drove the distinctions between factors. Based on these findings, a series of confirmatory factor analyses (CFA) and exploratory structural equation modeling (ESEM) analyses were computed first in the training sample and then repeated in the testing sample. These analyses directly tested whether specific social attention factors might measure a broad social attention factor (hierarchical), if a general social attention factor independent of specific factors provides better fit (bifactor), or if only correlated specific factors produce optimal fit. CFA is a more parsimonious model and, as such, only allows indicators to load onto the hypothesized factors. This can result in biased parameter estimates and poor overall fit. ESEM is advantageous in that indicators are permitted to cross-load on other factors while attempting to maintain low loadings (Asparouhov & Muthén, 2009; Marsh et al., 2014). Both models permit estimation of hierarchical and bifactor solutions. All models were estimated in MPlus version 7.2 using maximum likelihood estimation allowing for missing data; the ESEM model used GEOMIN rotation. Model fit was evaluated using recommended fit indices: The Comparative Fit Index (CFI), the Tucker-Lewis Index (TLI), the root-mean-square error of approximation (RMSEA), and the Standardized root-mean-square residual (SRMR). The following cut-offs across the fit indices were applied: (a) CFI and TLI values >0.90 indicate adequate fit and > 0.95 excellent fit; (b) RMSEA <0.08 indicates adequate fit and < 0.06 excellent fit, with 90% confidence intervals required not to cross the 0.08 boundary and the close fit test to have a *p* value >0.05; (c) SRMR <0.08 (Hu & Bentler, 1999; Marsh et al., 2004). Bifactor models have been criticized for over-fitting and capturing unwanted noise (Bonifay et al., 2017). For this reason, explained common variance

for the general factor and omega reliability for the general and specific factors was computed (Rodriguez et al., 2016).

To evaluate cross-cultural differences, linear and quadratic effects of age (age and age²), and the influences of sex and diagnosis (NT, DD, ASD) on social attention, generalized estimating equation (GEE) models were computed with the above variables as fixed effects factors. General social attention and specific factor scores were the dependent variables in separate analyses. General social attention was computed by first standardizing indicator scores and averaging across all indicators (after inversion of negatively-weighted indicators). Specific factor scores were computed as unit-weighted linear composites scores to allow reporting in the original fixation time percent metric. This approach was chosen rather than using factor scores from the best-fitting model because this approach allows for specific factors to be expressed in the fixation time percent metric and would make it easier to score these measures in future research and clinical practice. GEE models were estimated using maximum likelihood and fit was considered by iteratively examining alternative covariance structures (Hanley et al., 2003). Final models were presented based on independent covariance structure and a linear link function.

To evaluate the potential screening and diagnostic validity, data were evenly split into training ($n = 256$; neurotypical controls $n = 66$; DD $n = 63$; ASD $n = 127$) and testing ($n = 256$; neurotypical controls $n = 79$; DD $n = 59$; ASD $n = 118$) subsamples from the combined US and Qatar data. This was done because there were no major differences in structural models or mean values across samples, the Qatar sample had a limited number of non-ASD DD participants, and the goal was to develop the most generalizable model for evaluating case separation. There were no significant differences in age, sex, race, ASD sex ratio, autism traits, clinician-rated autism symptom severity, diagnostic group distributions, tracking ratio, number of valid stimuli across the training and testing sub-samples ($p > 0.05$). Support vector machine (SVM) analyses were estimated in the training sample and predicted probabilities were computed in the testing sample. Screening validity was evaluated by estimating the model with any DD as the dichotomous outcome (0 = no DD, 1 = any DD including ASD). Diagnostic validity was evaluated by estimating the model with any ASD as the dichotomous outcome (0 = neurotypical controls or other DD, 1 = any ASD). In both models, all 34 original AOI indicators, including those with low communalities and fixation time percent values that were excluded from factor analysis. Receiver operating characteristic (ROC) curve analyses examined the validity of predicted probabilities against the appropriate test variable (any DD or any ASD). The R source code is available from the first author upon request.

GEE analyses used SPSS version 26 and SVM and ROC analyses used e1071 and pROC (Robin et al., 2011) in R version 3.6.1. Recommendations for evaluating test

validity (STARD; Table S2) (Bossuyt et al., 2003) and reporting the results of a multivariate prediction model (TRIPOD; Table S3) (Collins et al., 2015) were followed for SVM and ROC analyses. Statistical significance was set at $\alpha = 0.05$, two-tailed. Power to detect significant factor loadings (>0.30) was excellent (>0.95). Power to detect significant covariate effects equivalent to partial $r_{ab,c} \geq 0.15$ in GEE models was excellent (>0.92). ROC analyses had good power (≥ 0.84) to detect an $AUC \geq 0.60$.

RESULTS

Participant characteristics

Most participants ($n = 512$ of 601; 85%) completed a valid eye-tracking assessment (Figure S2). The Qatar sample was older on average by 1.2 years, had a greater proportion of intellectual disability diagnoses within the DD group, and ASD cases had greater autism symptoms by parent report but not clinician observation (Table 1). The lack of ADHD or anxiety diagnoses in the Qatar sample is likely due to referral patterns. There were no sample differences in tracking ratio or number of valid stimuli from the remote eye tracking evaluation.

Structure of social attention

The best-fitting model in both the training and testing sub-samples was a bi-factor exploratory structural equation model with a general social attention factor and six specific factors (Figure 1; Table S4—model 6e). The general social attention factor explained 45% of the common variance in gaze indicators and included positive loadings from high social salience areas-of-interest (upper face, whole face, people vs. restricted interests) and negative loadings from low social salience areas-of-interest (lower face, body, and abstract vs. social preference). Four of the six specific factors (upper face, lower face, whole face, and body) included gaze indicators from multiple stimulus paradigms, suggesting that these social attention sub-components represent common patterns of attentional focus. Omega reliability was very good for the general social attention factor (0.87) and adequate to good for specific factors considering the small number of indicators for each factor (0.58–0.79).

Cross-cultural differences

US and Qatar samples did not show any significant difference in the general social attention factor (Figures 2a and S3, Table S5). However, there were some differences across specific factors. Namely, Qatar participants tended to look less at upper face regions ($d = -0.25$) but more at people vs. restricted interest images ($d = +0.30$) and body regions ($d = +0.23$). These differences were not

TABLE 1 Participant characteristics

	US M (<i>SD</i>)	Qatar M (<i>SD</i>)	χ^2/t (<i>p</i>)	Cohen's <i>d</i>
Total <i>N</i>	272	240	88.26 (<.001)	0.61
Healthy controls (<i>n</i> , %)	61 (22%)	84 (35%)		
Developmental disability (<i>n</i> , %)	110 (40%)	12 (5%)		
Autism spectrum disorder (<i>n</i> , %)	101 (38%)	144 (60%)		
Age (range)	6.5 (3.3, 1.5–18)	7.7 (3.6, 1.4–16)	3.97 (<0.001)	–0.35
Female (<i>n</i> , %)	65 (23.9%)	75 (31.3%)	3.47 (0.062)	0.17
Healthy controls (<i>n</i> , %)	22 (36%)	38 (45%)	20.42 (<0.001)*	0.28
Developmental disability (<i>n</i> , %)	23 (21%)	6 (50%)		
Autism spectrum disorder (<i>n</i> , %)	20 (20%)	31 (22%)		
ASD sex ratio (female: male)	1: 4.1	1: 3.7	0.11 (0.743)	0.03
White non-Hispanic (<i>n</i> , % US only)	203 (74.6%)			
Other diagnoses (<i>n</i> , %)			12.00 (0.017)	0.32
Language or communication disorder	58 (53%)	11 (92%)		
DD/ID	18 (17%)	2 (17%)		
Anxiety disorder	46 (42%)	0 (0%)		
Attention-deficit/hyperactivity disorder	35 (32%)	0 (0%)		
Other	41 (37%)	1 (8%)		
SRS-2 total T-score				
Healthy controls	45.4 (9.7)	45.4 (3.8)	0.01 (0.988)	0.01
Developmental disability	66.6 (12.7)			
Autism spectrum disorder	68.4 (10.8)	72.9 (12.3)	2.70 (0.008)	–0.38
ADOS-2 total severity (autism cases only)	6.3 (2.3)	6.1 (2.1)	0.62 (0.538)	0.09
Overall tracking ratio (%)	79.3% (13.5%)	79.1% (14.3%)	0.19 (0.847)	0.02
Number of valid stimuli (out of 44)	35.7 (7.6)	35.3 (7.9)	0.63 (0.529)	0.06

Note: Chi-square test examines the three-way cross-tabulation between cohort (U.S., Qatar), sex, and diagnosis. DD/ID = developmental delay/intellectual disability. In the Qatar sample, SRS Total T-score was estimated using Social Communication (SCQ) total raw scores based on a regression formula derived using a sample of 6700 cases with SRS and SCQ scores from the Interactive Autism Network. SRS Total T-score predicted = 42.878 + 1.806 * SCQ total raw score. The bivariate correlation between SRS Total T-score and SCQ total raw score is $r = 0.866$ indicating that these measures are largely redundant. SRS sample sizes were: US $n = 199$, Qatar $n = 214$. ADOS-2 Total Severity sample sizes for ASD cases were: US $n = 95$, Qatar $n = 92$. Due to IRB limitations, other developmental disability diagnoses were only documented for a sub-set of non-ASD cases in the US sample. The Chi-square statistic for comparing other developmental disability diagnoses across samples was converted to Cramer's *V*. As an effect size metric, Cramer's *V* is roughly equivalent to r and, therefore, to provide a common metric was converted from Cramer's *V* to Cohen's *d* via r . Only four SRS-2 scores were available in non-ASD cases in the Qatar sample. As a result, the mean and standard deviation for this group are not reported. Participants can have more than one other diagnosis, thus Other diagnoses do not add to the total number of cases.

accounted for by age, sex, or diagnostic differences across samples.

Age and sex effects

Overall, social attention remained stable, with only slight, nonsignificant increases across age (Figure 2b). Females showed a significantly stronger social attention preference ($d = +0.28$), and this preference was fairly consistent across all specific social attention factors (Figure 3a–f).

Diagnostic differences

DD cases had a significantly lower social attention preference than NT ($d = -0.10$ to -0.26). ASD patients had even lower social attention preference than DD cases, with predominantly medium-sized differences ($d = -0.29$

to -0.56) relative to NT. SRS-2 and ADOS-2 scores were significantly negatively correlated with general social attention ($r = -0.26$, $p < 0.001$ and $r = -0.12$, $p = 0.040$, respectively) and showed the expected pattern across specific factors (Table 2).

Using all available indicators, support vector machine model probabilities were trained and tested against any DD (including ASD) and ASD-only criteria to determine whether social attention patterns may be useful in screening for DD and identifying ASD. In the test sample, probabilities showed very good ability to predict any DD (AUC = 0.80) and good ability to predict ASD-only diagnosis (AUC = 0.76; Figure 4).

DISCUSSION

This is the largest study to characterize the structure of social attention, with a general social attention factor

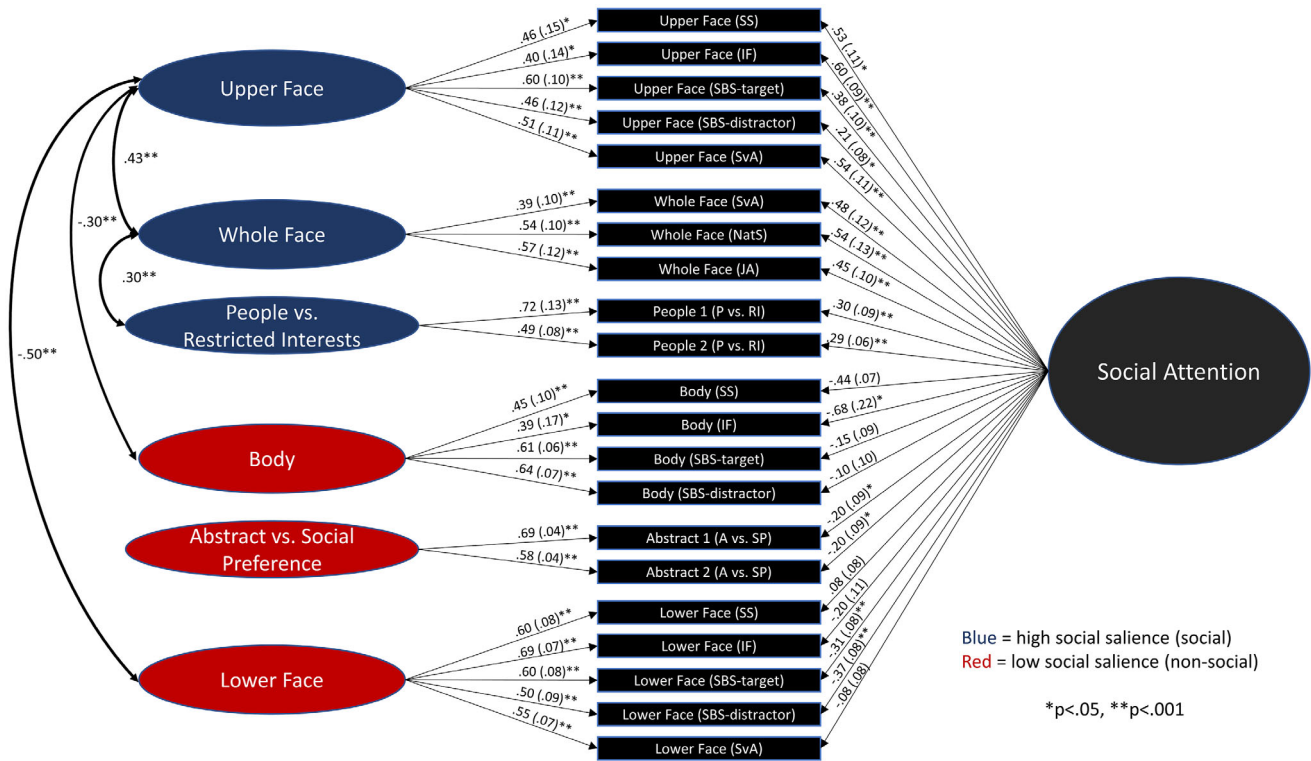


FIGURE 1 Structural model of gaze data across paradigms. Structural model depicts an exploratory structural equation bi-factor model with six specific factors and one general social attention factor in the total sample $N = 512$

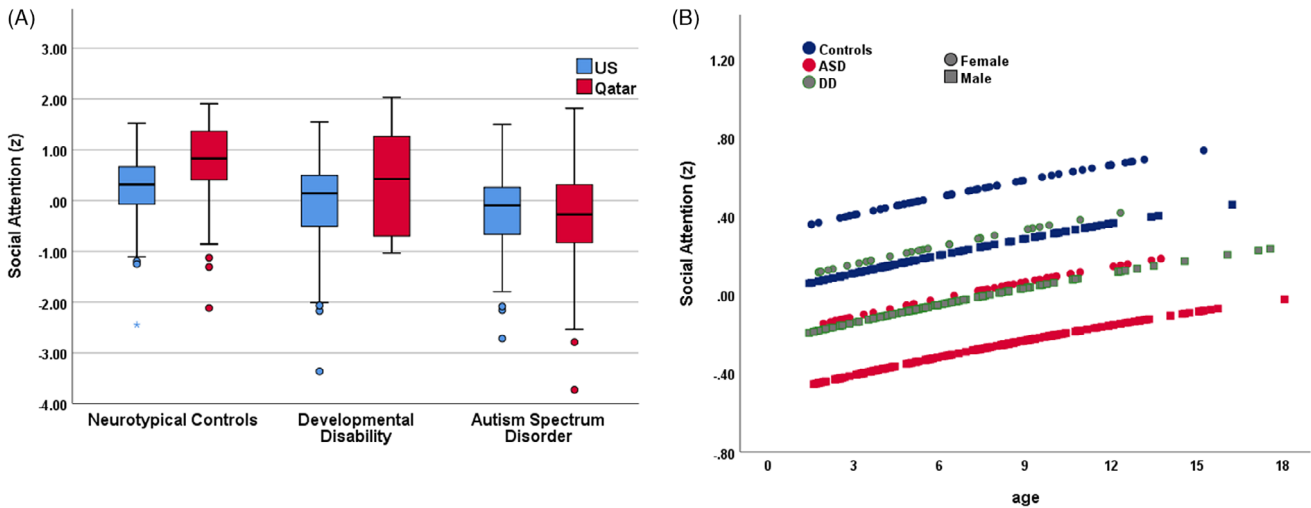


FIGURE 2 Boxplot (a) of social attention by United States and Qatar samples and diagnostic group. Regression plot (b) of social attention across age, separately by sex and diagnostic group. In the boxplot, the US sample is depicted in blue and the Qatar sample in red. In both plots, the diagnostic groups are neurotypical control, developmental disability, and autism spectrum disorder

emerging across multiple distinct social paradigms, consistent with results from a prior study in an infant/toddler sample (Chawarska et al., 2016). To our knowledge, this is also the only study to examine the cross-cultural consistency of a general social attention dimension. A cross-culturally consistent and stable social attention factor meshes closely with recent findings regarding an early

developing, genetically-mediated gaze preference to social information (Constantino et al., 2017), albeit with substantial variation across individuals and between typical and atypical neurodevelopmental groups. Specific attentional patterns showed cultural influences (e.g., less upper face looking in Qatar participants), possibly due to cultural norms in looking behavior toward adults,

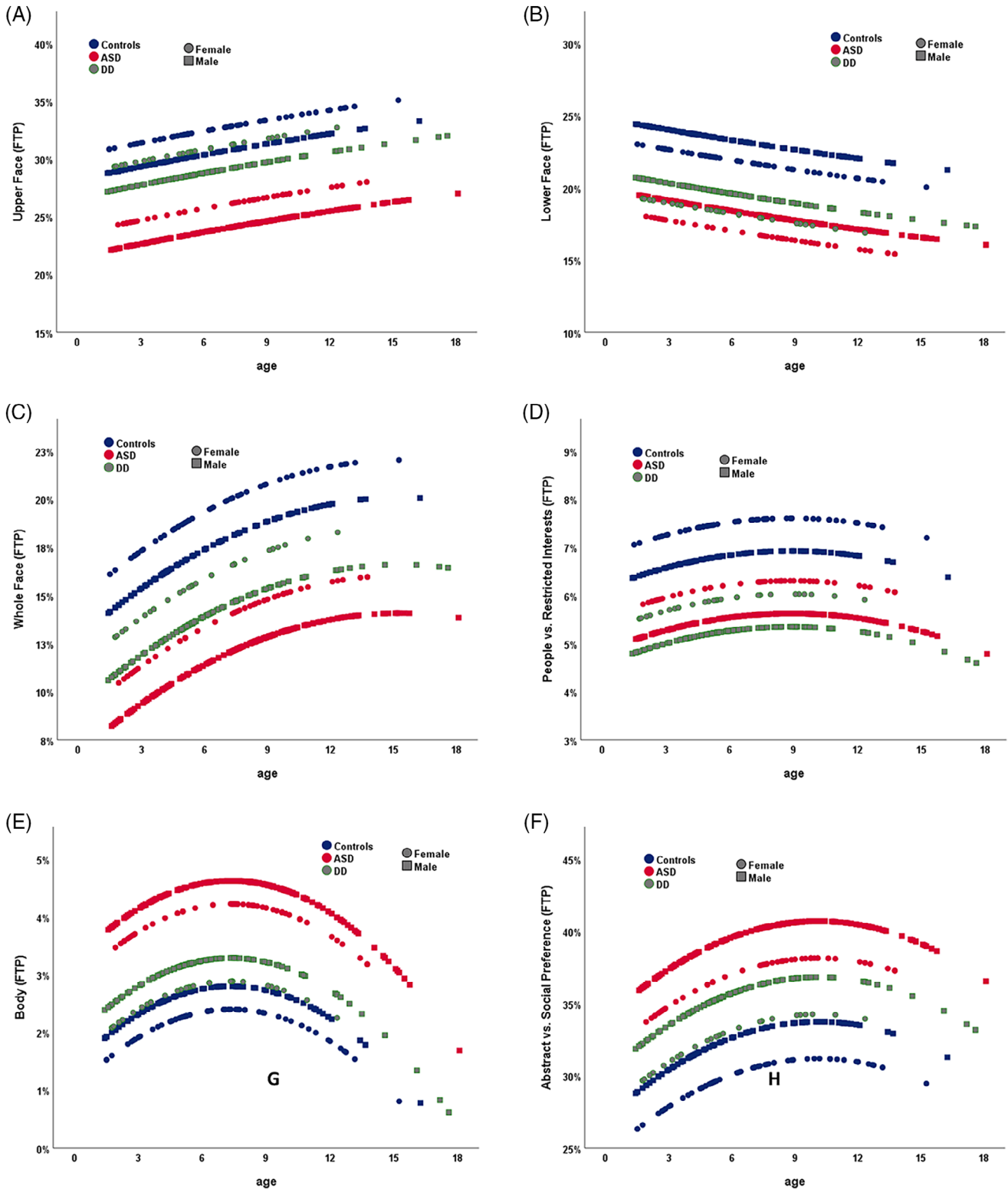


FIGURE 3 Regression plots for social attention sub-components (a–f) across age, separately by sex and diagnostic group. Regression plots depict predicted scores from generalized estimating equation models

consistent with the high Power Differential Index in Hofstede’s research. However, these differences tended to be minor, despite Qatar and the US having large cultural differences on several dimensions related to interpersonal

functioning (Han et al., 2013; Hofstede & Bond, 1984; Minkov & Hofstede, 2011). The more general pattern of preference to high social salience information remained consistent across cultures and stable across childhood.

The present study also identified social attention as a potential transdiagnostic neurodevelopmental risk marker, consistent with prior meta-analytic findings suggesting small reductions in DD cases and medium-to-large reductions in ASD (Frazier et al., 2017). Further research is needed with DD groups, but the present results suggest a gradient of social attention that spans typical and atypical development. This gradient was not due to model overfitting and accounted for a substantial

amount of variance in social attention indicators and is highly reliably measured. While more construct validation within specific RDoC processes is essential, it is possible that social attention measures may provide a key bridge between neural systems and behavior for several RDoC domains. For example, recent studies have suggested that attention to high and low social salience information may relate to RDoC social communication and habit sub-constructs, respectively (Frazier et al., 2016; Frazier et al., 2018; Sasson et al., 2008). Social attention factors may be particularly useful for understanding reception of facial and non-facial information within the social communication construct. Future research evaluating relationships between social attention and specific RDoC constructs will help to clarify how early social attention patterns influence related aspects of development.

TABLE 2 Correlations between social attention and autism symptom measures

	SRS-2 total T-scores	ADOS-2 total raw scores
Social attention	-0.26*	-0.12**
Upper face	-0.26*	-0.18**
Whole face	-0.30*	-0.20*
People vs. restricted interests	-0.14**	+0.02
Body	+0.20*	+0.12**
Abstract vs. social preference	+0.25*	+0.13**
Lower face	-0.13**	-0.07

Note: Bivariate Pearson correlations (*r*) are presented. Social attention, upper face, lower face, whole face, and people versus restricted interest-specific factors are expected to show negative correlations reflecting weaker attention to high social salience stimuli in those with higher autism symptoms. In contrast, body and abstract versus social preference factors are expected to show positive correlations reflecting more attention to low social salience in those with higher autism symptoms.

p* < 0.001; *p* < 0.05.

The fact that females show consistently stronger social attention than males is in line with better neurodevelopmental outcomes in females during childhood (Barbu et al., 2011; Zablotsky et al., 2019). Females show earlier and stronger social development (Barbu et al., 2011), including greater social communication skills (Frazier et al., 2014), and appear to be relatively protected from ASD and related neurodevelopmental conditions (Zablotsky et al., 2019). Prior research suggests that stronger social attention in females is observable even in neonates (Connellan et al., 2000). As an early-developing cognitive process, social attention differences are likely to be a key early mediator of later differences in more complex social behaviors, such as

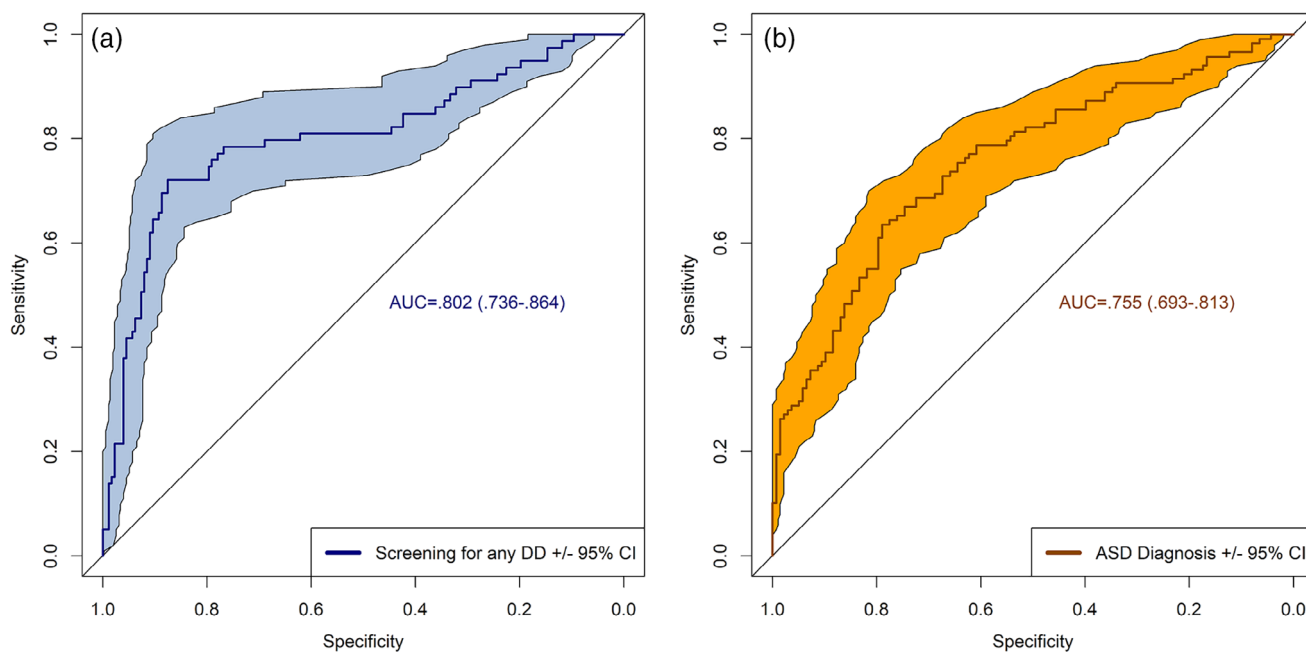


FIGURE 4 Receiver operating characteristic curves with support vector machine model probabilities predicting any developmental disability (a—blue) and autism spectrum disorder diagnosis (b—orange). Support vector models are based on all gaze indicators were first estimated in the training sub-sample (*n* = 256) and then validated in the test sub-sample (*n* = 256)

perspective-taking and reciprocal interaction. Future research characterizing sex differences and clarifying longitudinal relationships with more complex social behaviors will be important for identifying early intervention strategies that maximize social outcomes. A recent study identified that females with ASD showed stronger attention to some types of social information than males with ASD, and that females with ASD had generally equivalent social attention to typically-developing males (Harrop et al., 2019). The present study did not include sex by diagnosis interaction in the statistical analysis plan but post hoc evaluation indicated that this interaction was only significant for the upper face region, reflecting larger differentiation in looking to upper face regions between NT males and females than for males and females in non-ASD and ASD groups.

Several specific social attention factors were found to be paradigm independent (upper face, lower face, whole face, and body) and these dimensions showed distinct relationships with age, sex, and diagnosis. This suggests that, beyond a general social attention factor, there are other reliable gaze patterns that children used to perceive their worlds. These patterns may provide specific information about other's internal states and intentions (upper face, whole face) (Emery, 2000), movements (body) (Betti et al., 2019), or track speech production (lower face) (Tenenbaum et al., 2013). Further investigation is needed to replicate and extend the bifactor model of social attention to other cultures, paradigms, and stimuli. Intriguingly, in the present study, the lower face region had generally negative loadings on the social attention factor. However, the loading for the single speaker indicator was positive and the loading for individual facial expressions was negative but small and non-significant. This pattern likely reflects the fact that the lower face region can become socially salient during perception of speech (Grossman et al., 2015) or specific types of facial expressions (Pritsch et al., 2017).

General social attention and specific social attention factors were moderately associated with autism traits and showed small (mostly nonsignificant) relationships with autism symptom severity. The magnitude of these relationships is partly a function of imperfect reliability in both variables (social attention factors and autism traits/symptoms) but also suggests that general social attention and social attention factors, individually, are not sufficiently strong to predict autism traits/symptom severity. In contrast, results of the present study suggest that combining these factors may provide greater validity in predicting autism. Specifically, combining all gaze indicators from the social attention factors using machine learning methods, showed good accuracy in screening for any DD and in identifying ASD cases. The relatively inexpensive and easy-to-collect nature of social attention measures suggests that they may have cross-cultural value for screening and clinical evaluation. As ASD and other neurodevelopmental disorders are identified

and treated earlier, tracking social attention may also be useful for evaluating early intervention progress. The present results supply initial age and sex-adjusted norms for evaluating a child's social attention relative to expectation. Future research is needed to collect larger norms, develop more accurate algorithms, and conduct further cross-cultural validation.

The primary limitations were a modest sample size for DD cases in the Qatar sample, relatively limited coverage of mid-to-late adolescence in both samples, confirmation of NT cases only by parent report, and the necessary focus on only seven social stimulus paradigms. Future research is needed to address these limitations, replicate social attention structure across additional cultures and other race/ethnicity groups in the U.S., further delineate age and sex effects, and more accurately map the boundaries between typically-developing and DD cases. This research should include additional stimulus paradigms, including direct interaction paradigms which may be more sensitive to developmental differences (Chevallier et al., 2015) or may represent a different aspect of social attention (Grossman et al., 2019), to evaluate generalizability and look for other stimulus-independent social attention factors.

In conclusion, the present study identified a general social attention factor that was cross-culturally-consistent, stable across age, and showed substantial individual variation across typical and atypical development. Beyond replication, future research is needed to longitudinally track social attention, other social cognitive functions, specific social behaviors, and social outcomes to more clearly elucidate how these domains interact to produce social competency or, when dysfunctional, social impairment. This research has the potential to inform RDoC social processes, explicate the role of social development in developmental psychopathology, and generate new measures for identifying neurodevelopmental disorders.

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CONFLICT OF INTEREST

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ETHICAL APPROVAL

The Cleveland Clinic and Qatar Biomedical Research Institute IRBs reviewed and approved the research protocols.

AUTHOR CONTRIBUTIONS

Thomas W. Frazier had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Concept and design: Thomas W. Frazier and Mirko Uljarevic. Acquisition, analysis, or interpretation of data: All authors. Drafting the manuscript: Thomas W. Frazier. Critical revision of the manuscript for important intellectual content: All authors. Statistical analysis: Thomas W. Frazier and Mirko Uljarevic. Obtaining funding: Fouad A. Al-Shaban, Mohammed Aldosari, and Thomas W. Frazier. Administrative, technical, or material support: Al-Shaban. Supervision: Fouad A. Al-Shaban, Thomas W. Frazier, and Mohammed Aldosari.

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SUPPORTING INFORMATION

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