Physiological responses to social and non-social stimuli in neurotypical adults with high and low levels of autistic traits: Implications for understanding non-social drive in Autism Spectrum Disorders.

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Lay Abstract:

Theories suggest that symptoms of autism spectrum disorders (ASD) arise from a reduced interest in social activities and a drive towards non-social activities. This research investigated how these atypical interests are related to differences in emotional responses to non-socially related objects (for example trains) compared with responses to faces. A non-ASD population was recruited for this study, and their autistic traits were measured using the Autism Spectrum Quotient (AQ) questionnaire. They were then shown images of different items, including pictures of non-social objects (e.g. cars), as well as pictures of faces, while their emotional response was monitored using a device that measures arousal through increases of sweat on the skin. The results showed that participants with a higher number of autistic traits had a significantly higher response to the non-social images than they did to faces, and the greater the difference between response to non-social and social images. This is the first time a study has demonstrated a relationship between autistic traits and emotional response to images of objects, suggesting that such a response may underlie the drive towards non-social systems that could result in the symptoms of restricted interests and repetitive behaviours in ASD.
**Scientific Abstract:**

Researchers have suggested that the two primary cognitive features of ASD, a drive towards non-social processing and a reduced drive towards social processing, may be unrelated to each other in the neurotypical (NT) population and may therefore require separate explanations. Drive towards types of processing may be related to physiological arousal to categories of stimuli, such as social (e.g. faces) or non-social (e.g. trains). This study investigated how autistic traits in an NT population might relate to differences in physiological responses to non-social compared with social stimuli. NT participants were recruited to examine these differences in those with high vs. low degrees of ASD traits. 46 participants (21 male, 25 female) completed the Autism Spectrum Quotient (AQ) to measure ASD traits before viewing a series of 24 images while skin conductance response (SCR) was recorded. Images included 6 non-social, 6 social, 6 face-like cartoons and 6 non-social (relating to the participants’ personal interests). Analysis revealed that those with a higher AQ had significantly greater SCR arousal to non-social stimuli than those with a low AQ. This is the first study to identify the relationship between AQ and physiological response to non-social stimuli and a relationship between physiological response to both social and non-social stimuli, suggesting that physiological response may underlie the atypical drive towards non-social processing seen in ASD and that at the physiological level at least, the social and non-social in ASD may be related to one another.
1. Introduction

1.1 ASD and the Social Brain

Criteria for diagnosis of autism spectrum disorders (ASD) include impaired social communication and non-social repetitive and restrictive behaviours, with the broader diagnosis of ASD intended to recognise that these symptoms represent a continuum or spectrum ranging from mild to severe (American Psychiatric Association, 2013). Twin studies have indicated that the social and non-social behaviours, though both highly heritable, may be genetically independent of one another and benefit from being considered separately (Ronald, Happé and Plomin, 2005; Happé, Ronald and Plomin, 2006).

Traditionally, a great deal of research into ASD has focused on the social aspect of the disorder, with much attention being paid to the areas of the brain involved in emotion and face recognition and processing. These brain structures include the amygdala and the fusiform face area (FFA), which various studies have shown to be abnormal in ASD (Brothers, 1990; Baron-Cohen et al., 2000; Bookheimer, et al., 2008; Ashwin, et al., 2007; Schultz, 2005; Boucher, et al., 2005; Gaigg and Bowler, 2007; Howard, et al., 2000; Kanwisher, et al., 1997; Pierce, et al., 2001; Critchley, et al., 2000; Schultz, et al., 2003). However some studies suggest a different picture of the function of these brain areas in ASD. One fMRI study found that there were no significant differences in FFA activation between adults with ASD and controls when shown facial stimuli in comparison with non-social stimuli (Hadjikhani, et al., 2004), suggesting that the social deficits in autism are due to the overall dysfunction of a distributed social processing network in the brain rather than abnormal functioning in a particular area. A second study found that there was no difference in performance on non-social amygdala-related tasks between those with ASD and controls (South, et al., 2008). This suggests that impairment of the amygdala in ASD is specific to
social information. An fMRI study on a child with ASD discovered activation of both the FFA and the amygdala when he was shown images of Digimon characters, which were an example of his particular restricted interest (Grelotti, et al., 2005). The child did not show activation of these areas when viewing images of faces, suggesting that while the areas of the brain usually associated with social processing may be intact in ASD, they may instead be activated by non-social stimuli, or stimuli specific to a particular obsession or special interest.

1.2 Restricted Interests and Repetitive Behaviours: The Non-Social in ASD

The mechanisms underlying the non-social core diagnostic criterion for ASD (restricted interests and repetitive behaviour) are less frequently studied, although more recently the importance of researching this aspect of ASD’s cognitive profile in order to better understand the etiology of the condition has been highlighted (South, et al., 2005). It has been postulated that this characteristic of ASD represents an overdeveloped drive to construct and analyse rule-based systems, or extreme ‘Systemizing’. Systemizing has been contrasted with Empathizing, deficits in which account for the social difficulties characteristic of ASD (Baron-Cohen, 2002; 2009). The Empathizing-Systemizing (E-S) theory of autism posits that the spectrum of autistic traits extends from those with few autistic symptoms (good social communication, no repetitive and restrictive behaviours) through the ‘typically developing’ (TD) population to those with mild, and then severe, ASD (impaired Empathizing with preserved or enhanced Systemizing).

As highlighted by Happé et al., (2006) there is little evidence to show how these different features of ASD (social impairment or lack of Empathizing, and repetitive/restricted behaviours or Systemizing) are related to one another or whether they can even be explained by a single theory. They argue that cognitive theories of autism (such as the E-S theory), while often able to explain the social deficits of ASD, cannot account for the non-social aspects of the disorder; and those theories that adequately explain repetitive and restricted
behaviours are unable to provide a satisfactory account of how they relate to social difficulties. In a previous twin study, Ronald et al., (2005) found that while both social and non-social behaviours in TD 7 year old twins are highly heritable, they do not appear to be related to one another at the genetic level. This raises the question of how these co-occurring behaviours interact with each other in ASD, and at what level, if any, they are related, and therefore whether they should be studied separately.

Happé et al. suggest that due to the requirement of both these social and non-social characteristics for a diagnosis of ASD, studies to establish whether these core features are indeed fractionated or have a unitary explanation need to be carried out on the general population. This is made possible by the fact that the behavioural traits of ASD can be found to a greater or lesser extent among neurotypical individuals, forming a continuum, or ‘autistic spectrum’ as described by Baron-Cohen (2002). The Autism Spectrum Quotient (AQ) was designed to assess the degree of autistic traits in adults with normal intelligence and can therefore be used to measure where an individual lies on this spectrum (Baron-Cohen, et al., 2001a).

The concept of Systemizing provides explanatory power when addressing the issue of talent in autism (Baron-Cohen, et al., 2009). While ASD is a debilitating disorder in general, there is strong evidence of normal or higher than normal cognitive ability in ASD when it comes to certain tasks that involve deriving rules or patterns in non-social systems (Shah & Frith, 1983; Jarrold, Gilchrist, & Bender, 2005 Baron-Cohen S. et al.,2001b; Brosnan, et al., 2010; 2014). Music is a prime example of a rule-based system, and one that frequently elicits an emotional response in the typically developing population (Levitin, 2006). Research indicates that people with ASD show intact or superior musical pitch processing (Heaton, et al. 1998) and that they are able to identify the emotional content of music, a ‘complex non-social affective stimulus’ (Caria et al., 2011).
There is growing evidence to suggest that autistic individuals are in fact able to recognise both ‘non-social’ (e.g. fear or happiness) and ‘social’ (e.g. guilt or embarrassment) emotions in others under experimental conditions (Williams and Happé, 2010; Hobson, et al., 2006). The authors of these studies acknowledge that while autistic individuals may possess cognitive processes for recognising emotions similar to non-autistic individuals, it is clear that they cannot apply these processes flexibly across a variety of contexts in daily life. For example, it may be that the focused and systematic structure of the experimental tasks facilitates that processing, while the pressures and complexities of real life situations makes social emotional processing particularly difficult for those with ASD.

While social emotional processing in ASD is invariably affected in everyday contexts, the ability to recognise social emotions in experimental conditions, and the ability to identify the appropriate emotional content of music suggest that ASD may not involve a complete deficit in emotion recognition and processing. In another study, autistic adults and adolescents demonstrated intact learning and perception of emotionally relevant non-social stimuli equivalent to that of TD controls (South et al., 2008). This indicates intact amygdala function for other aspects of emotional processing and decision-making where social stimuli are not involved. There is anecdotal evidence to suggest that people who usually score highly on the AQ derive emotional pleasure from the predictability of physics and patterns in the world and have an emotional response to abstract concepts and systems (Baron-Cohen, et al., 2001a).

Emotional arousal to presented stimuli can be reliably assessed by measuring skin conductance response (SCR) (Greenwald, et al., 1989), and there have been several studies investigating SCR in ASD. For example, Hubert, et al. (2009) performed a study guided by the somatic marker hypothesis, which suggests that autonomic arousal to stimuli plays a crucial role in directing attention and influencing decision-making (Damasio, 1996). They found that adults with ASD exhibited lower SCRs to emotional faces than typical matched
controls, while performing similarly on emotional expression judgement tasks. This suggests that while social judgements may be mediated by physiological arousal in the TD population, those with ASD employ different strategies to achieve similar results. SCR could therefore be an important measure of individual differences in the kinds of processing elicited by different categories of stimuli.

Gaigg and Bowler (2007) demonstrated atypical fear acquisition in ASD, with participants exhibiting attenuated autonomic fear responses in comparison to TD controls, and similar autonomic responses to both conditioned and non-conditioned stimuli. This suggests poor connectivity between the amygdala and other regions of the brain, leading to abnormal processing of the emotional significance of sensory stimuli. The authors suggest this may underlie the behavioural characteristics and social deficits seen in ASD.

A recent study by Stagg, et al. (2013) investigated the relationship between language development and arousal to faces and eye gaze in children with ASD, finding that SCRs to faces differentiated ASD children from the TD control group, and that arousal to faces also differentiated late and normal language onset among the ASD group. These results appear to confirm results from previous studies demonstrating hypoarousal to faces among ASD individuals (Dalton, et al., 2005; Kylliäinen & Hietanen, 2006), as well as providing evidence that there is a relationship between SCR to social stimuli and language development.

Stagg et al. explain their results by suggesting that a relationship between higher arousal to faces and the quality of eye contact in early infancy may confer an advantage for language development in children with ASD. However, this study did not use non-social stimuli as a control measure, so these results could alternatively be explained if ASD participants display hypoarousal to all forms of stimuli in general, or alternatively if there are other kinds of stimuli that elicit ‘normal-’ (in comparison to TD arousal to faces) or hyper-arousal. It is
therefore important for studies of this kind to investigate arousal to different kinds of stimuli in order to understand more fully the role of arousal in the social deficits of ASD.

Despite a number of other studies investigating physiological responses to social stimuli in ASD (Blair, 1999; James & Barry, 1984; Baron-Cohen, 2009; Kylläinen & Hietanen, 2006), as yet no substantial research has been undertaken to assess emotional response to the non-social in ASD. The aim of the present study was to investigate the mechanisms behind the non-social features of ASD by analysing physiological responses to both social and non-social stimuli, and to identify the possibility of a relationship between response to these two categories of stimuli in the TD population (and therefore assessing their relatedness as suggested by Happé et al.).

In line with E-S theory, we hypothesised that those with a higher number of ASD traits would have a higher physiological response to non-social stimuli and a lower response to social stimuli, and we predicted a positive relationship between AQ and non-social stimuli of interest to the participant. We also predicted that the difference between arousal to social and non-social stimuli would be larger the higher the AQ, suggesting that the social and non-social are related to one another (and to AQ) in a TD population, and that difference in physiological response to social and non-social stimuli may underlie some aspects of the cognitive profile of ASD.

2. Methods

2.1 Participants

As participants in this study were recruited from the TD population, the AQ was used to assess whether there was any difference in results between those scoring higher on the AQ and those with a low score. If ASD is indeed at the extreme end of a spectrum on which we all lie, results from this study should provide an indication of how people with ASD respond to social and non-social stimuli. 46 neurotypical participants aged between 18
and 66 years ($M=26.7$ years), (25 female ($M=26$ years), 21 male ($M=28$ years)) were analysed, and were recruited from the University of Bath population through the Department of Psychology electronic notice board and posters displayed around campus. Participants were provided information on the basic background of the study (without mention of ASD) and what was involved before giving their consent. The experiment was conducted in two parts; the first part involved completion of an online survey and the second part was carried out in a quiet laboratory on campus. Participants had to complete the online survey before coming to the lab for testing, where they were each paid £5 on completion of the tests. The study was approved by the University of Bath, Department of Psychology Ethics Committee.

2.2 Autistic traits – the AQ

Participants were administered the full 50 item Autism Quotient questionnaire (Baron-Cohen, et al., 2001) as part of an online survey that also established age, gender and non-social objects of interest. The survey was created and run between December 2011 and August 2012 using Bristol Online Surveys (2012). Answering each question on the survey was mandatory, so there were no missing data for any participants completing it. The results were scored according to Baron-Cohen et al.’s specifications, resulting in an ‘AQ score’ for each participant.

2.3 Stimuli

Each participant was shown a total of 24 images. Each image belonged to one of four conditions: Social - Face, Social-Cartoon, Non-Social and Non-Social of Interest. There were 6 images in each condition. Images in the Social-Face condition were sourced from an online database (Tarr, 2012), images in the Social-Cartoon condition were sourced from previous research that had identified the emotion in the cartoon could be reliably recognised by those with ASD (Brosnan et al., 2013). The Non-Social and Non-Social of Interest images were freely available for use and sourced from the Google Images search engine (Google, Inc).
Images chosen for the Non-Social condition were items or objects that neither involved any human nor animal subject, and were not the subject of any participant’s interest. The images included: a bicycle; a paintbrush; a car; a paperclip; a train, and a telescope. The online survey included several questions about the participants’ own hobbies and interests, how much time and money they spent on their main hobby and the objects that they most associated with it. Relevant images were then selected for presentation in the control condition of the electrodermal analysis section of the study on the basis of this survey. Each image was converted to greyscale, sized to 100 pixels per inch, cropped and centred on a white background with a width of 20cm and a height of 10cm using Adobe Photoshop CS5 software (see Figure 1).

**Figure 1 about here.**

The experiment was built and run using the E-Prime® 2.0 suite of applications. The order of stimulus presentation was initially randomised and each participant was shown images in that order. Individual Non-Social of Interest stimuli were changed for each participant according to images selected for them on the basis of their interest. Each stimulus was presented on screen for 5 seconds. The inter-stimulus interval (ISI) varied randomly between 8-12 seconds, with a mean ISI of 10 seconds over the whole procedure in accordance with previous studies (Breska, et al., 2010). A fixation in the shape of a small cross appeared in the centre of the screen during each interval.

2.4 Skin Conductance Response

Skin conductance response (SCR) was chosen as the measure of emotional arousal to visual stimuli, in line with previous studies (Greenwald et al., 1989). A Biopac GSR100C was used to measure skin conductance. An emotional or physiological response was deemed to have occurred when there was a rise in the amplitude of the skin conductance level of at
least 0.01 μS within 1-4 seconds of a stimulus onset (Dawson, et al., 2007; Venables & Christie, 1980).

Acqknowledge™ 4.1 software was used to calculate SCRs from the recorded skin conductance level of each participant. SCRs were measured by comparison to a localized baseline that was established by the software using median value smoothing. The calculation of skin conductance amplitude was determined by the change in the amplitude of the skin conductance level from the time of the SCR onset to the maximum amplitude attained during the SCR (see Biopac Systems, Inc.).

2.5 Procedure

Participants were seated on an adjustable chair in an acoustically and electrically sealed booth, approximately 60 cm from a 20inch Dell monitor, with a keyboard positioned in front of them on a small table. An isotonic gel was applied to the Biopac EDA finger transducer which was attached to the distal phalanx of both the fore and middle finger of the dominant hand in accordance with recommendations (Screbo et al., 1992).

The on-screen instructions told the participant to passively view each image and to ensure they remembered each in preparation for a memory test at the end. This was included as an incentive for the participants to pay attention to stimuli in what was an otherwise passive task.

2.6 Analysis

Electrodermal activity (EDA) was analysed for each participant from the recording using the Acqknowledge™ 4.1 software. The initial sampling rate was 1kHz, but due to high frequency noise obscuring the signal, the SCR waveform was downsampled to 30 samples/second to capture the true nature of the signal, and was ‘cleaned up’ by running a 1hz FIR low pass filter, as instructed by Biopac technical support (pers. comm).
If a stimulus did not elicit a response according to the parameters described above, then this was recorded as a zero response. Log of (SCR +1) was calculated across all responses as recommended when including these zero responses. A mean SCR magnitude was calculated for each participant, for each condition (Dawson, et al., 2007). To correct for individual differences in skin conductance level between participants, the mean SCR magnitudes for each condition were transformed into z-scores and these were used in the statistical analysis.

2.7 Statistical Analysis

The data were explored using IBM SPSS Statistics 19 and the alpha was set at 0.05. A Shapiro-Wilk test revealed that all data for the transformed mean SCR magnitudes for each of the four conditions were not normally distributed (for all conditions, p<0.05), and the data were unable to be transformed into a normal distribution. Non-parametric tests were therefore employed in analysis. A one-tailed bivariate Spearman correlation was run to explore the relationship between AQ and mean SCR magnitude to each condition. To explore the average difference in arousal to non-social images compared with the response to social images, the transformed mean SCR magnitudes for the social condition were subtracted from those for the non-social condition.

3. Results

Five participants were excluded from analysis as the SCR data were incomplete due to a technical problem resulting in no recorded SCR response to any of the conditions, leaving a total of 46 participants for analysis (25 female, 21 male). The mean age for the final group was 27 (SD=10) and the mean AQ was 18 (SD=7). An independent-sample t-test revealed that there were no significant gender differences in AQ (t (44) = -.59, p=.558). Table 1 shows the means for SCR magnitude to each of the stimulus conditions.

Table 1 about here.
For the whole group AQ was significantly positively correlated with mean SCR magnitude to non-social stimuli \((r=.407, p=0.002)\). There was also a significant negative correlation between AQ and social (cartoon) stimuli \((r = -0.312, p = 0.017)\). AQ was not significantly correlated with mean SCR magnitude to either the non-social stimuli of interest or social (faces) conditions (both \(p > 0.05\)) (see Figure 2). . .

**Figure 2 about here.**

In addition there was a significant correlation between mean SCR magnitude to non-social of interest and social (faces) conditions \((r = 0.317, p = 0.016)\) and between the mean SCR magnitude to social (faces) and social (cartoon) conditions \((r = 0.424, p = 0.002)\).

Finally, there was also a correlation between AQ and the average difference in mean SCR magnitude to all non-social images compared with that to all social images \((r = 0.267, p = 0.036)\), indicating that the greater the AQ, the larger the gap between the higher response to the non-social and the lower response to the social (see Figure 3).

**Figure 3 about here.**

4. Discussion

The results of this study largely support our initial hypotheses, finding that those reporting a higher number of autistic traits have higher physiological arousal to non-social stimuli than those reporting fewer autistic traits. The correlations suggest that the higher the AQ, the greater the physiological response to non-social stimuli, and the higher the AQ, the greater the difference between physiological response to non-social compared with social stimuli. However, the results do not support our hypothesis that AQ would be negatively correlated with SCR to social stimuli, and we would have also expected a correlation between AQ and arousal to the non-social items of interest, which was not found. The possible reasons for this are discussed below.
The finding that AQ is positively correlated with arousal to non-social stimuli demonstrates, we believe for the first time, a connection between high self-reported autistic traits in a TD population, and a greater physiological response to the non-social. Although further research is needed to tease out the nature of this relationship, it suggests that physiological response may underlie the development of certain traits and behaviours seen in ASD, including poor or limited social functioning, and restricted and repetitive behaviours.

This finding, along with the negative correlation found between AQ and mean SCR magnitude to the cartoon condition, supports the theory that physiological arousal to social and non-social stimuli differs across the normal range of ‘the spectrum’, as it is defined by the E-S theory. Those self-reporting more ASD traits (higher Systemizing, lower Empathizing) display greater arousal to the non-social condition than those with a lower AQ, and those with fewer ASD traits (i.e. higher Empathizing, lower Systemizing) display greater arousal to abstract social images (in the case of cartoons) than those with a higher AQ. If these results extend to an ASD population, physiological response to non-social stimuli could be part of the mechanism underlying both enhanced Systemizing and reduced Empathizing in ASD.

That there was no correlation between AQ and the non-social of interest condition, contrary to our prediction, is possibly due to the participants’ anticipation that this type of item would appear during the task eliciting a higher average response across all participants regardless of AQ (given that they had been asked in advance to provide details of their non-social interest). After having undertaken the task, several participants commented on seeing the images relating to their interest and sometimes mentioned that the wrong type or make of item had been used. Therefore it would seem that these stimuli may have elicited a reaction across all participants that was not necessarily related to interest, but to anticipation, or the
recognition that this image was ‘for them’ and in some cases that the image was not ‘correct’ in their view.

We had hypothesised that those with a higher number of autistic traits would show larger responses to personal non-social items of interest, in line with evidence from the study by Grelotti, et al. (2005) that showed a ‘social’ response in the brain of an autistic child when viewing images of his special interest. It may be, however, that in TD individuals the kind of interest invested in non-social items or activities is not of the same quality or intensity as that of the autistic individual and their special restricted interests, which form a crucial part of an autism diagnosis.

It may therefore be the case that while there exists a relationship between AQ and arousal to non-social items in general, this relationship breaks down in a TD group for non-social items of interest when the responses of the whole group rise. As TD individuals, this increased arousal may be due either to heightened attention to an object of interest (in line with the somatic marker hypothesis), or due to other factors as mentioned above. To investigate the relationship between AQ and arousal to non-social stimuli of personal interest more comprehensively, future similar studies looking at a TD population will need to find a way of minimizing the potential influence of such factors.

The significant relationship between arousal to non-social of interest stimuli and the response to human faces could be explained by the inherent interest of faces to a neurotypical population, and the personal interest in items relating to each participant’s hobby. It would therefore make sense that in this sample of TD adults, those who are highly responsive to items that interest them are also highly responsive to faces. As noted above, it is possible that the arousal to the items of interest was in part due to anticipation or recognition of the personal nature of the images, in which case this correlation may be explained individual differences in responsiveness to salient stimuli.
As discussed above, research conducted by Ronald et al. (2005) found that there was little genetic overlap between social and non-social behaviours, but the present study found that there is a significant negative relationship between the social and non-social in a neurotypical population, in terms of physiological response. If this apparent relationship between physiological response to the social and the non-social is not accounted for at the genetic level, then it is possible that these responses are experientially related, or learned, at least in a TD population.

As previously mentioned, the fusiform face area is activated when typically developing subjects view social stimuli, but can also be activated in ASD subjects when viewing images related to their special interest (Grelotti, et al., 2005; Critchley, et al., 2000; Kanwisher, et al., 1997). The suggestion from this previous research is that areas of the brain involved in face processing may not actually be specialized for faces in particular, but for areas of expertise. The results from the current study suggest that physiological response could be related to what it is that we become experts in.

Evidence suggests that having a physiological response to faces may result in increased attention to faces, thus resulting in having expertise in facial expressions and their emotional significance. For example Dalton, et al. (2005) demonstrated a link between arousal to faces and the time spent looking at them, and the study by Stagg, et al. (2013) suggested that the relationship they found between arousal to faces and language onset in ASD children could be due to the effect arousal to faces may have in directing attention towards them at an early age, facilitating language development. Conversely, having an increased physiological response to non-social stimuli such as geometric shapes, recurring patterns or rule-governed systems may result in increased attention to such stimuli, the consequence being an increased ability or drive towards such objects and systems. If arousal is related to attention towards a particular domain, such as people or systems, and thus related to cognitive ability in, or drive
towards, that domain, then this could explain why the social and non-social traits of ASD have low genetic heritability in the general population, yet remain related to one another. If there is a primary cognitive drive towards one particular domain (either social or non-social), it makes sense that the other is less likely to elicit as strong a response.

Further research therefore needs to establish whether increased physiological arousal increases attention or vice versa. The results of this current study provide a foundation for further exploration of physiological responses to non-social stimuli in an ASD population; future studies are needed to investigate the relationship between attention to both social and non-social stimuli and physiological response in ASD and TD samples to determine whether autonomic arousal to non-social stimuli plays a role in the restricted interests and repetitive behaviours characteristic of autism.
References


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Figures

Figure 1. Example of Social-Face, Non-Social and Social-Cartoon stimuli used in the experiment

Figure 2. Mean SCR Magnitude for each condition plotted against AQ score

Figure 3. Difference in mean SCR magnitude between total non-social and total social conditions
Table 1: Total mean SCR magnitude for each condition (with standard deviations in parentheses)

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N=46