I want to reiterate my warmest thanks to Niclas Öberg and the LifeWatch foundation for their support of my research.

During the past two years, my work has centered on one big question: ***why is eye-contact such a big problem for individuals with autism?*** And the answer is probably: because they are over-sensitive to direct gaze, that is perceived as a threat, and this results in their avoidance of eye-contact, in order to handle the overwhelming emotional reaction it provokes. This efficient strategy however comes at a price, because of the importance of information that is carried by the eyes during social interaction, and not looking at eyes and faces leads to the improper development of the social brain.

In the first study that we published on this topic [1], we took an indirect measure of the development of the social brain by examining how face viewing is modulated by the emotional expression of the stimuli, using eye-tracking. In a relatively large group of individuals with (n=57) and without ASD (n=58), we demonstrated that face-viewing is flexible and varies as a function of emotion in typical individuals, but that it is less the case in children/adolescents with ASD - or in typical young people who score high on the Autism Quotient (AQ), a measure of autistic traits - who adapt less in their face perception as a function of emotional content.

The second study was about the effect of constraining gaze in the eyes on brain activation in typical individuals [2]. In this experiment, we used functional brain imaging (fMRI) and compared what happened when participants looked at short videos of emotional faces either in a free viewing paradigm, or with their gaze constrained in the eye region through the presence of a cross between the eyes of the stimulus. Note that besides the cross, the stimuli were absolutely identical. What we demonstrated was that there was significantly increased activation of the ‘social brain’ when these typical participants were constrained to look in the eyes, and that the degree of amygdala connectivity with the rest of the brain was increased for all emotions except for fear. Amygdala connectivity was also modulated by the level of anxiety, alexithymia and autistic traits, for each different emotion in a specific way. For example, when watching *angry* faces in the eyes, the more participants had autistic traits, the strongest was the amygdala connectivity with areas of the social brain.

The third study [3] was probably the most exciting one, as for the first time we were able to demonstrate a substrate for the difficulties encountered by autistic individuals in engaging in eye-contact. Using the same paradigm as the one used in the study described above, we showed that constraining gaze in the eye-region provoked abnormally high activation of the so-called subcortical face processing system, that consists of the superior colliculus, the pulvinar nucleus of the thalamus, and the amygdalae. The subcortical system is very interesting, as it is the starting point for the development of face specialization and is sensitive to direct gaze. What our data showed was that the subcortical system in ASD over-reacts not only to threat stimuli, but also to stimuli that one would consider as positively engaging and socially rewarding such as happy faces. Our results indicate that ASD individuals, contrary to what many have thought, do not have a fundamental lack of interpersonal interest, but quite the opposite: they are in fact *oversensitive to socio-affective stimuli*, as our previous work on empathy in autism had demonstrated. This lack of looking in the eyes is actually an attempt that ASD individuals use to decrease arousal, as direct gaze, regardless of the emotional expression, is experienced as a threat. While avoiding gaze is a good strategy to avoid stress, it comes at a price, since the eyes carry such important interpersonal and deictic information during social interaction and communication and may lead to the improper development of the social brain that arises from gaze avoidance.

Finally, in our latest study [4], we used static stimuli of emotional faces, but this time faces expressed these different emotions at different intensities. It is indeed rare in real life to have people express emotion in the exaggerated way that is usually seen on faces in datasets used to probe emotional processing. Therefore, we created new stimuli showing only 40% of the full intensity emotion, and compared brain activation of 27 ASD individuals with 21 typical controls for these stimuli, constraining gaze with a fixation cross in the eye region. What we discovered was that individuals with ASD actually had more amygdala activation than typical controls when they were perceiving fear expressed at low intensity. We also observed that there was less activation in ASD compared with controls in an area of the brain important for emotional regulation. Our conclusion from this study was that there is an imbalance between the excitatory and the inhibitory system in socio-affecting processing in ASD, which could result in the social disengagement and avoidance of eye-contact.

The results from these different studies show that gaze avoidance in ASD results from an attempt to reduce stress, and not from indifference. They also show, together with other studies that we and others have performed in the past, that the social brain of individuals with autism works differently than that of typical individuals. We believe that this is the result of not having normal eyes and face experience during development, due to eye-contact avoidance. We now want to explore whether there are ways that we can use to try to help ASD individuals to be less stressed by eye-contact, in order to circumvent the cascade of events leading to the improper development of the social brain that arises from gaze avoidance and to help them in daily life interactions.

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