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DISSERTATION

"The conscious and unconscious processing of socially relevant visual stimuli"

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1 Abstract

The efficient processing of socially relevant information is critical for successful social interactions. The aim of this thesis was to investigate the extent to which the processing of socially relevant information depends on awareness using a combination of behavioural and neural data. Study 1 used eyetracking in healthy human participants to provide empirical evidence that eye gaze, an inherently salient social cue, influences ongoing behaviour in the absence of awareness and showed an unconscious bias towards direct gaze. Study 2 explored the neural mechanism behind this preferential processing of direct gaze. Finally, Study 3 used classical conditioning to ascribe salience to a stimulus and showed that eye movements were not preferentially directed to a fear-conditioned stimulus, in the absence of awareness. Taken together, these studies exhibit the profound influence of inherent social relevance on human behaviour while at the same time demonstrating the limits to which complex information can affect human behaviour outside awareness. They further offer a promising platform for new interventions in disorders characterized by impaired social interactions and investigations into the behavioural and neural effects of other ecologically relevant stimuli.

Abstrakt

Die effiziente Verarbeitung von sozial relevanten Reizen ist entscheidend für erfolgreiche soziale Interaktionen. Das Ziel der vorliegenden Arbeit war es, zu untersuchen, inwieweit die Verarbeitung von sozial relevanten Informationen vom visuellen Bewusstsein über diese Informationen abhängt. In Studie 1 wurde Augenbewegungsmessungen durchgeführt um empirische Beweise dafür zu liefern, dass Blickkontakt - ein sozialer Reiz, der sich durch eine inhärente Salienz auszeichnet - laufendes Verhalten in Abwesenheit von Bewusstsein beeinflussen kann. In dieser Studie zeigten gesunde Teilnehmer eine Präferenz für Blickkontakt, obwohl sie die präsentierten Gesichter nicht bewusst wahrnehmen konnten. Studie 2 untersuchte den neuronalen Mechanismus, der dieser bevorzugten Verarbeitung von Blickkontakt in gesunden Teilnehmern zugrunde liegt. In Studie 3 wurde die soziale Relevanz eines Reizes mittels klassischer Konditionierung manipuliert. Hier zeigte sich, dass in Abwesenheit von Bewusstsein Augenbewegungen nicht bevorzugt auf den konditionierten Reiz gelenkt wurden. Zusammengefasst zeigen diese Studien den Einfluss von Reizen mit inhärenter sozialer Salienz auf das menschliche Verhalten. Zugleich zeigen sie aber auch, dass die Effekte sozialer Informationen auf das Verhalten außerhalb des visuellen Bewusstseins begrenzt sind. Sie stellen weiterhin eine Grundlage für neue Interventionen bei psychiatrischen Erkrankungen, die soziale Interaktionen betreffen, sowie für Untersuchungen zu Verhaltens- und neuronalen Effekten anderer ökologisch relevanter Reize dar.

2 Introduction

Every minute we are confronted with large amounts of sensory information. Due to the brain's limited processing capacity, at a given point of time only a small amount of the available information is actually processed and influences our behaviour. It therefore becomes crucial to prioritize relevant information in order to react appropriately. What constitutes relevant information? In most situations, visual information gains relevance based on its emotional (spiders, snakes), social (faces), or motivational (reward, punishment) meaning. For example, human faces constitute highly relevant stimuli due to the wealth of information they convey. In particular, humans are sensitive to the information present in the eyes as they provide information about others' emotions, intentions, and focus of attention (Kleinke, 1986). Direct gaze, which develops into mutual eye contact, is often the precursor to a social interaction. It is a form of social reward (Kampe et al., 2001) and captures spatial attention in a fast and reflexive manner (Senju and Hasegawa, 2005). In addition to this involuntary capture of attention, direct gaze also influences complex, high-level cognitive functions such as gender discrimination (Macrae et al., 2002), face recognition, memory (Hood et al., 2003; Mason et al., 2004) and decision making in social contexts (Snyder et al., 1974). The importance of direct gaze to social interactions is further highlighted by the fact that atypical eye contact is the primary hallmark of psychiatric disorders that are characterized by impairments in social interactions like autism (Tanaka and Sung, 2013) and social phobia (Horley et al., 2003). While eye gaze is an inherently relevant stimulus that receives preferential processing and affects subsequent behaviour, stimuli can also acquire relevance through learning or conditioning. In classical conditioning, first introduced by Pavlov in 1927, formerly neutral stimuli can gain relevance when they are paired with an aversive or pleasant event. Such conditioned stimuli also capture and modulate attention (Armony and Dolan, 2002; Mulckhuyse and Dalmaijer, 2015) and are more easily detected (Padmala and Pessoa, 2008) compared to neutral stimuli.

From an evolutionary perspective, it would be biologically advantageous to rapidly detect highly relevant information from the environment in order to immediately react to it. This is, for instance, critical for survival in the case of threatening stimuli and for successful social interactions. Such rapid detection mechanisms necessitate that some information is processed before it reaches consciousness. Especially the development of new methods has facilitated the investigation of behavioural and neural responses to stimuli presented below the limen of consciousness (Kim and Blake, 2005). Two common approaches to assess unconscious visual processing include measuring (i) the time until an initially unconscious stimulus reaches awareness (access to awareness) and (ii) behavioural or neural responses while a stimulus is completely suppressed from awareness.

Using the first approach, it has been shown that socially salient information (direct gaze, fearful faces, etc.) that is initially suppressed from awareness, gains access to awareness faster over non-salient information (review: Yang et al., 2014). While access to awareness has often been used as a proxy for unconscious processing, this relation has recently been questioned (Stein and Sterzer, 2014). Instead, differences in the time to reach awareness between stimuli could reflect differences in the transition phase, that is, the period of partial awareness when the stimulus is gradually becoming conscious. Thus, an account based on access to awareness alone does not provide unequivocal evidence for unconscious processing.

Related to the second approach mentioned above, behavioural and neural responses have been observed for emotionally relevant stimuli that were presented for very brief durations (Dimberg and Öhman, 1996; Morris et al., 1999). However, in these cases, unawareness of the stimuli was simply assumed based on the short presentation times. These studies have therefore been criticized for not directly assessing observers' awareness (Lovibond and Shanks, 2002; Pessoa, 2005). Furthermore, behavioural responses to suppressed stimuli, usually recorded as button presses, are often recorded after a particular stimulus has been presented. Thus, the extent to which highly relevant information can be processed outside of awareness and influence ongoing behaviour, that is, during the presentation of the suppressed stimulus, has remained elusive.

The investigation of behavioural responses to subliminal stimuli thus necessitates (i) a masking technique to reliably suppress stimuli and (ii) a response measure that can be recorded simultaneously, which also (iii) allows for the assessment of participants' awareness. Firstly, the method of continuous flash suppression (CFS; see section 4) has proven effective to render stimuli invisible for prolonged periods of time (Tsuchiya and Koch, 2005). Secondly, eye movements provide a continuous measure of participants' behaviour while stimuli are suppressed from awareness using CFS (Rothkirch et al., 2012). Since eye movements reveal the observer's focus of attention, a bias in eye movements towards a particular stimulus indicates the observer's preference for this stimulus over another in the absence of awareness. Furthermore, eye movements allow the simultaneous assessment of observers' awareness usually indicated by button presses. A large number of studies till date only use subjective reports for the assessment of awareness. They are, however, prone to response biases (Kunimoto et al., 2001). This implies that participants' might hesitate to indicate that they saw a stimulus when the available evidence is weak. In contrast, a bias-free measure can be obtained using objective criteria. Here, participants are considered unaware of a stimulus only when their performance in a discrimination or detection task is not different from chance. Objective criteria in combination with subjective confidence reports can provide more reliable measures of awareness (Sterzer et al., 2014). While we now have a sensitive measure to assess awareness and an online marker to assess the influence of socially relevant stimuli on behaviour and neural responses outside awareness, direct evidence for such processing remains to be investigated.

3 Objective

The aim of this doctoral thesis was to investigate the extent to which the processing of acquired and inherent socially salient visual information depends on awareness. We used eye gaze as a proxy for an inherently salient stimulus and studied the behavioural biases to direct gaze present in typically developed (TD) volunteers. We next investigated the neural responses to eye gaze under varying levels of awareness in TD participants and finally probed the influence of acquired stimulus salience on eye movements outside of awareness. Together, the studies aim at providing a deeper understanding about our behavioural and neural sensitivity to socially relevant stimuli and the extent to which such information is processed outside of awareness. They are also intended to lay the foundation for subsequent research and new interventions on understanding gaze processing in psychiatric disorders that are characterized by impairments in social interactions. The individual studies shed light on the following questions:

1. Are eye movements biased towards faces with direct gaze in typically developed participants despite unawareness of the faces? (Study 1)
2. How are the neural responses to eye gaze modulated by participants' awareness of the faces? (Study 2)
3. Can attention be biased towards unconscious fear-conditioned stimuli presented outside of awareness? (Study 3)

4. Methods and Results

For the studies that make up this thesis, a combination of different methods was used. These include the combination of continuous flash suppression (CFS) with eye tracking (Studies 1 to 3), functional magnetic resonance imaging (fMRI) (Study 2), and skin conductance (Study 3). The methods and stimuli used are described in detail in the publications listed in the appendix. This section briefly explains each of these methods before concluding with a summary of the design and results of each individual study.

Continuous flash suppression (CFS): Participants' awareness was manipulated using the interocular suppression technique CFS. In CFS, the two eyes are presented with two different visual inputs. The dominant eye is presented with high contrast, dynamic, mask stimuli flashed at a high frequency (10Hz in the current studies) while the non-dominant eye sees a static, low-contrast stimulus of interest. The two images are fused with the help of a mirror stereoscope (in Studies 1 and 3) or an fMRI compatible cardboard divider (Study 2) such that the percept of the participant is predominantly that of the mask stimuli while the stimulus of interest is suppressed from awareness. The low contrast stimuli of interest in the following Studies were faces: neutral faces with different eye gaze direction in Studies 1 and 2 and fearful faces in Study 3.

4.1 Data acquisition and analyses

Assessment of Awareness: In all the studies that comprise this thesis, the experimental trial concluded with two questions that were used to assess participants' awareness of the presented stimuli based on both subjective and objective criteria. The first question was a 2-alternative forced choice task (2AFC) in which participants had to indicate the interval in which the stimuli were presented (temporal 2AFC: Studies 1 and 3) or the location of the stimulus (spatial 2AFC in Study 2). The second question was a four-point confidence rating scale, where participants indicated their confidence in their 2AFC decision. Confidence rating scales provide a good reflection of participants' subjective awareness of stimuli and are commonly used for this purpose (Zehetleitner and Rausch, 2013). Trials were first classified as aware or unaware based on participants' subjective confidence ratings. In a second step, a bias-free measure of awareness was obtained from the analysis of participants' task performance in the 2AFC task in those trials in which they indicated unawareness of the stimuli: Task performances at chance level were taken as an indication for complete unawareness of the stimuli. The main analyses were either only performed on unaware trials (Studies 1 and 3) or unaware trials were contrasted against aware trials (Study 2).

Eyetracking: Eye movements in Studies 1 and 3 were recorded with a high-speed video-based eye tracker manufactured by Cambridge Research Systems with a sampling rate of 250Hz. In the fMRI experiment (Study 2), an MRI compatible, infrared video eyetracker manufactured by SensoMotoric Instruments (SMI IVIEW X™ MRI-LR) with a sampling rate of 50Hz was used for this purpose. Video-based eye trackers use infrared lights to illuminate the eye, which creates corneal reflections (Figure 1). The movement of the corneal reflections relative to the pupil is used to compute the current gaze direction. The acquired data, which were saved as x (horizontal position) and y (vertical position) coordinates, were pre-processed and analysed in Matlab. Prior to the start of data acquisition, a calibration procedure was performed for every participant. This procedure involved the recording of eye movements from a known set of target positions such that accurate measurements of subsequent pupil and corneal positions could be recorded.

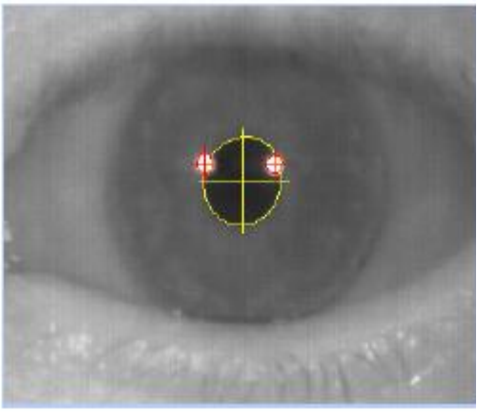

***Figure 1**: Tracked pupil and corneal reflections (white spots) from a video based eye tracker sampling at a frequency of 250Hz. Image adapted from Video Eyetracker Toolbox user manual v 3.11.*

In Studies 1 and 3, eye movement data were analysed to identify saccades. In contrast, in Study 2, eye movements were tracked to ensure that participants were able to maintain central fixation during stimulus presentation so that neural responses elicited by the different stimulus conditions were not confounded by the simultaneous activity due to eye movements.

Functional Magnetic Resonance Imaging (fMRI): For Study 2, fMRI data were acquired on a TRIO 3T scanner manufactured by Siemens, Erlangen, Germany. Functional T2*-weighted MR images were acquired using an Echo Planar Imaging (EPI) sequence. Whole-brain coverage was obtained with 38 contiguous slices (voxel size: $3 \times 3 \times 3$ mm³).

Additionally, for each participant T1-weighted structural images (MPRAGE, voxel size 1 × 1 × 1 mm^3) were also acquired.
FMRI data were analyzed using SPM 8 for Matlab. Pre-processing of the functional images involved slice-time-correction, realignment to correct for head motion, co-registration of each participant's structural to the functional images, segmentation of grey and white matter, and spatial normalization to the MNI space. In the final step, all normalized images were smoothed with an 8-mm full width at half-maximum Gaussian kernel. Statistical analyses of the functional images were performed in two steps. The first step involved analyses at the subject level where the effect of the experimental conditions in each voxel was estimated in the context of a general linear model. The contrast estimates obtained from the first level were then subjected to a group level analysis. Our main regions of interest (ROI) included the fusiform face area (FFA), the superior temporal sulcus (STS), amygdala and intraparietal sulcus (IPS), regions known to be involved in eye gaze processing (Senju and Johnson, 2009). To individually identify the face-responsive voxels in our ROIs, we additionally performed a functional face localizer in every participant.

Skin conductance: Electrodermal activity in Study 3 was recorded with the Vision Recorder software manufactured by Brain Products GmbH, Munich, Germany, to determine the physiological arousal to an aversively conditioned stimulus. Two silver-silver chloride (Ag-AgCl) electrodes were filled with standard electrolyte paste and placed on the distal phalanges of the second and third fingers of the left hand. The skin conductance response originates from the autonomic activation of the sweat glands in the skin. Increased arousal causes an increase in the moisture secreted by the sweat glands, resulting in changes in the electrical characteristics of the skin. Data were acquired in micro-Siemens (µS) with a sampling rate of 500Hz. The acquired data was analysed using the Matlab based software Ledalab. Data pre-processing comprised downsampling, filtering, and artefact correction. A continuous decomposition analysis was then performed on the pre-processed data to separate tonic skin conductance activity from the phasic responses to the stimuli.

4.2 Participants, Design and Results of the Individual Studies

4.2.1 Study 1: "Making Eye Contact Without Awareness" *(Rothkirch*, Madipakkam* et al., 2015, Cognition)*

The aim of this study was to investigate whether eye movements in typically developed (TD) adults are biased towards faces with a direct gaze even when these faces are presented outside of awareness.

Participants and Design: We performed two experiments with 34 and 31 participants respectively, without a history of psychiatric or neurological disorders. Each participant's dominant eye was determined prior to the start of the main experiment with an eye dominance test to increase the effectiveness of interocular suppression. In the main experiment, faces with direct and averted gaze were presented to the participants' non-dominant eye while CFS masks were concurrently flashed at a frequency of 10HZ to the dominant eye. The faces could be presented in one of two intervals. In experiment 1, the face stimuli were presented for the complete duration of the interval (800 ms) whereas, in experiment 2, the face stimuli were saccade contingent. This means that the stimuli were removed from the screen upon initiation of the first eye movement. Such a design reduced the risk that the stimuli might break into participants' awareness and because attentional effects to direct gaze are short-lived (Senju and Hasegawa, 2005). Participants were instructed to search for the faces by making eye movements. Stimulus presentation was followed by the assessment of awareness of the presented stimuli.

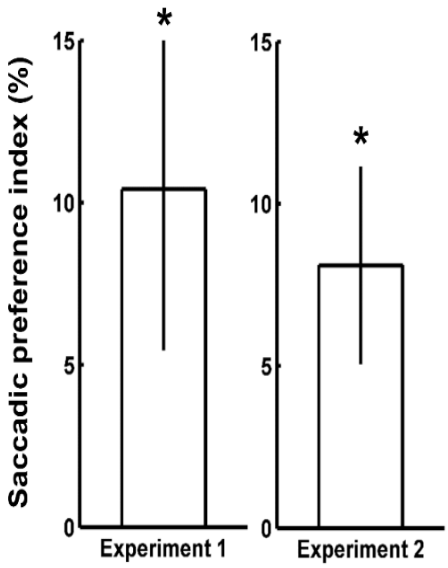

***Figure 2**: Significantly positive saccadic indices in experiments 1 and 2 indicate an unconscious bias towards direct gaze in healthy adults.*

Results: On average in 58.5% (± 4.7 SEM[1]) of trials in experiment 1 and 68.1% (± 4.5 SEM) in experiment 2, participants reported to be unaware of the stimuli. This was confirmed by chance performance in the 2AFC task (experiment 1: 50.5% (± 0.8 SEM); experiment 2:

[1] SEM: Within subject standard error of the mean (Cousineau, 2005)

48.9% (± 0.5 SEM); one-sample *t*-test against 50%: $p > 0.05$ in both experiments). A bias towards one of the two faces with different gaze directions was quantified for each participant in terms of a saccadic preference index. Positive indices indicate an attentional bias to the face with direct gaze, while zero indicates no preference to either gaze direction. The saccadic preference indices in both experiments were significantly above zero (Figure 2), indicating an unconscious bias to the face with direct gaze (experiment 1: 10.41% (± 4.95 SEM), $p = 0.046$, effect size $d = 0.41$; experiment 2: 8.10% (± 3.05 SEM), $p = 0.015$, effect size $d = 0.58$). In addition, in experiment 2 saccades towards the face with direct gaze tended to have shorter latencies than those made toward the averted gaze (437.90 ms (± 6.68 SEM) vs 462.45 ms (± 6.68 SEM)); paired sample *t*-test: $t(20) = -1.83$, $p = 0.08$, $d = 0.42$). The results of both experiments of Study 1 consistently demonstrate that TD humans have a preference towards faces with direct gaze even when they are completely unaware of these faces.

4.2.2 Study 2: "Gaze Direction Modulates the Relation between Neural Responses to Faces and Visual Awareness" *(Madipakkam et al., 2015, Journal of Neuroscience)*

Study 1 investigated the unconscious bias to eye contact in healthy adults and provided evidence that socially relevant stimuli can affect ongoing behaviour in the complete absence of visual awareness. In Study 2 we used CFS and functional magnetic resonance imaging to measure the neural responses to direct and averted gaze faces in relation to participants' awareness of the stimuli.

Participants and Design: We tested 21 participants using the same stimulus set as in Study 1. A face with either a direct or averted gaze was presented either to the left or right of a central fixation cross to the non-dominant eye of the participant. Participants' awareness of the face stimulus was manipulated by the simultaneous presentation of CFS masks to the dominant eye. Stimulus presentation was followed by a spatial 2AFC task and a confidence rating. To ensure that participants were able to hold central fixation, eye movements were recorded throughout the task.

Results: The distribution of participants' horizontal eye positions revealed no differences between the different conditions indicating that participants were able to maintain fixation equally well in all conditions. On average, participants reported to be unaware in 54.5% (± 4.08 S.E.M) of all trials. Average 2AFC performance in the unaware trials (59.23% (±

2.57 S.E.M)) was significantly reduced in comparison to aware trials (88.3% (± 2.77 S.E.M); $p < 0.001$). Furthermore, the number of unaware direct gaze trials was significantly less than the number of unaware averted gaze trials ($p = 0.028$). In other words, there was a preferential access to awareness for direct gaze.

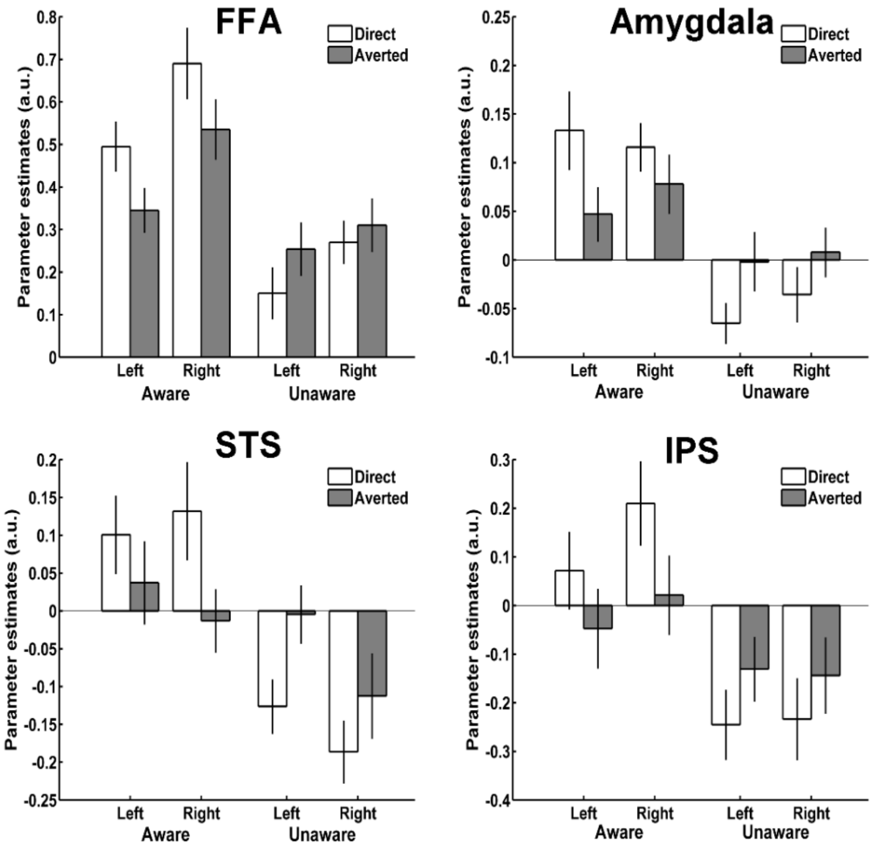

***Figure 3**: Neural responses to faces with direct and averted gaze direction in trials presented along with CFS masks. The main effect of awareness and interaction of awareness-by-gaze was highly significant in all four regions of interest*

With respect to the neural responses to direct and averted gaze, a 2 × 2 × 2 (rmANOVA[2]) with the factors awareness (aware/unaware), hemisphere (left/right) and gaze direction (direct/averted) was performed for each ROI (Figure 3). In all ROIs there was a significant awareness-by-gaze interaction effect (all $p_{corr} < 0.05$): neural responses to direct gaze were significantly larger compared to averted gaze when participants reported awareness of the faces, whereas unaware faces with direct gaze elicited smaller neural responses compared to averted gaze. Strong negative correlations in all ROIs, which was most robust in the FFA ($r = -0.69$, $p_{corr} = 0.01$), between the frequency of the awareness of faces with direct gaze and the corresponding neural responses, suggest that those participants with a strong preferential access to awareness for direct gaze became aware of these faces at lower neural activity levels relative to an averted gaze. This finding that lower levels of neural activity were sufficient to give rise to the awareness of a direct gaze

[2] repeated measures analysis of variance

face relative to an averted gaze, was further corroborated by an additional trial-wise analysis of the relationship between awareness and the neural responses to gaze.

4.2.3 Study 3: "Probing the influence of unconscious fear-conditioned faces on eye movements" *(Madipakkam et al., 2016, Consciousness and Cognition)*

Studies 1 and 2 used eye gaze, an inherently positive, salient, stimulus to investigate its processing with respect to visual awareness. In Study 3 we investigated the effect of acquired stimulus salience on eye movements in the absence of awareness. Stimulus salience was exploited using a classical fear- conditioning procedure.

Participants and Design: 29 participants took part in this study. The experimental design consisted of a conditioning phase and a test phase. In the conditioning phase, the presentation of one of two fearful face stimuli (CS+) was paired with an aversive noise (unconditioned stimulus: US) on 50% of trials, while the other face stimulus never occurred with a noise (CS-). Participants were instructed to passively view the stimuli while their skin conductance was recorded throughout stimulus presentation. This provided a measure of their autonomic arousal to the stimuli. In a subsequent test phase, the conditioned stimuli were presented simultaneously with CFS masks to render them invisible. The trial structure was similar to Study 1, where participants searched for the face stimuli (CS+ and CS-), which could be presented in one of two intervals, while their eye movements were being recorded. Awareness was assessed based on both subjective and objective criteria using a temporal 2AFC task and a 4-point confidence rating scale. The experimental session consisted of 10 runs which included 2 baseline pre-conditioning runs so that post-conditioning effects could be computed relative to the baseline. This was followed by alternating conditioning and test runs, four of each. Before the first pre-conditioning run and at the end of the last test run, participants were instructed to rate the intensity of the fearful expression of the face stimuli using a visual analog scale. The ratings provided a subjective measure of the effectiveness of the fear-conditioning procedure.

Results: Skin conductance responses (SCRs) in the unpaired CS+ trials were significantly larger than in the CS- trials ($p = 0.03$) (Figure 4), indicating increased physiological arousal to the fear-conditioned CS+ stimulus. In addition, there was also a change in the subjectively experienced affect induced by the stimuli. The perceived intensity of the fearful expression increased by 9.8% (± 2.9 SEM) for the CS+ stimulus, while it decreased by a similar value (9.7% (± 2.9 SEM)) for the CS- stimulus. This difference in the ratings of the two stimuli was statistically significant ($p = 0.003$). Analyses of eye movements only focused on those trials in which participants reported unawareness of the stimuli (least confident trials of the confidence rating scale). This was on average in 81.2% (± 2.4 SEM) of all trials. Manual 2AFC performance in the subjectively unaware trials was not significantly different from chance level, indicating that the face stimuli were effectively suppressed from awareness (49.52% (± 0.74 SEM); one-sample t-test against the chance level of 50%: $p > 0.5$). However, there was no saccadic bias to the CS+ face stimulus after conditioning ($p > 0.80$). Positive saccadic preference indices for both the CS+ (23.2% (± 6.3 SEM)) and CS- stimulus (19.9% (± 6.3 SEM)) suggested that the conditioning procedure caused a general increase in sensitivity to face stimuli. A positive correlation (Pearson's $r = 0.48$, $p = 0.02$ after the removal of two outliers) between the SCRs and the saccadic indices suggests that the attentional bias to the CS+ stimulus depended on the strength of the conditioned response, or in other words, the arousal induced by the stimulus in the participant.

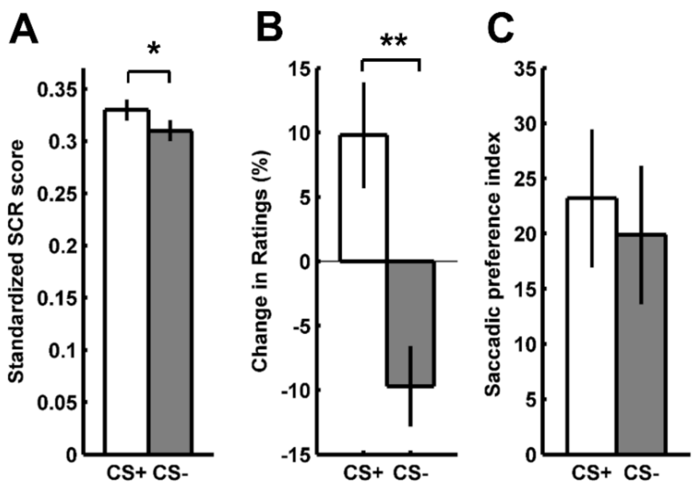

***Figure 4**: **(A)** SCRs elicited by the CS+ and CS- stimuli. **(B)** Significant difference in the change in subjective rating of the fearfulness of the face stimuli before and after conditioning. **(C)** No difference in the saccadic preference indices for the CS+ and CS- face.*

5 Discussion

The aim of this thesis was to investigate the extent to which the processing of acquired and inherently salient visual information depends on visual awareness. Studies 1 and 2 used eye gaze, a potent non-verbal social stimulus, to study both the behavioural and neural biases to eye contact in typically developed adults. Finally, Study 3 examined the influence of acquired stimulus salience on behaviour outside of awareness. In the following paragraphs, the main results of the individual studies will be briefly summarized again before being discussed. The chapter concludes with the relevance of the current findings and an outlook for future research.

Behavioural responses to direct gaze outside of awareness

Study 1 addressed the influence of direct gaze on the oculomotor system when it is suppressed from awareness. The results indicated that eye movements were preferentially directed to faces with a direct gaze, even though TD participants were completely unaware of these faces. The findings provide evidence for the unconscious processing of eye gaze and that socially relevant information affects ongoing behaviour in the absence of awareness. These results emphasize the importance of eye contact in human communication as the precursor to any social interaction where the rapid and automatic orientation towards direct gaze constitutes a biological advantage. This is further supported by the observation that even neonates orient preferentially towards direct gaze (Farroni et al., 2002). The findings of Study 1 contribute to the long standing debate on the extent to which complex information can influence behaviour unconsciously (Kouider and Dehaene, 2007). They go beyond the existing literature using reaction times to show a preferential access to awareness of direct gaze in TD adults (Stein et al., 2011). In contrast, the online assessment of eye movements as in Study 1 demonstrated behavioural biases towards socially relevant stimuli that are constantly suppressed from awareness, while simultaneously assessing participants' awareness of the stimuli using objective criteria. Currently, the neural model for the unconscious processing of eye gaze is hypothesized to involve a rapid subcortical face detection pathway involving the superior colliculus and amygdala which receives low spatial frequency information through the magnocellular pathway (Senju and Johnson, 2009). Indeed, the superior colliculus plays a critical role in the execution of eye movements (Isa and Hall, 2009) and recently, the amygdala was found to be activated in response to direct gaze in a cortically blind patient (Burra et al., 2013). Furthermore, the results of Study 1 emphasize the functional relevance of the subcortical pathway, which was previously thought to be only involved in the processing of emotion (Morris et al., 1999). Importantly, the results also offer a promising starting point for the understanding of gaze processing in autism and social anxiety disorder, where the avoidance of eye contact is one of the key diagnostic symptoms (Horley et al., 2003; Tanaka and Sung, 2013). Preliminary results from a study using the same design as Study 1, performed in clinically diagnosed patients with autism spectrum disorder (ASD) showed that while healthy controls had a bias towards suppressed faces with direct gaze, patients with autism had a bias towards the faces with an averted gaze indicating an unconscious avoidance of direct gaze. Critically, participants from both groups showed no differences in the total number of saccades that were made. These results provide the first evidence that eye gaze avoidance in autism is an unconscious, involuntary and automatic response, which significantly contributes to our understanding of the disorder.

Neural responses to eye gaze in dependence on visual awareness

While Study 1 explored the behavioural bias to eye contact when stimuli are continuously suppressed from awareness, Study 2 investigated the neural responses to eye gaze in relation to participants' awareness of the stimuli. The results of Study 2 showed that with increasing neural activation, direct gaze entered awareness more readily than averted gaze. Previous behavioural research has shown that direct gaze not only biases attention outside of awareness (results of Study 1), but also has the potency to enter awareness faster than averted gaze (Stein et al., 2011). The results of Study 2 provided evidence for the neural mechanism underlying this prioritized access to awareness of direct gaze by showing that direct gaze had a lower neural threshold for entering awareness compared to averted gaze. Higher neural responses were observed for direct versus averted gaze when participants reported awareness of the faces, whereas the opposite pattern was found when participants were unaware of the faces. Although increases in neural activity in the visual cortex as a function of awareness have been shown before for a variety of stimuli (Moutoussis and Zeki, 2002; Pessoa et al., 2006), the results of Study 2 demonstrated that this relationship between awareness and neural activity is modulated by eye gaze, a subtle but highly relevant social cue. The observation that direct gaze requires less neural activity to reach awareness could mean that the neural coding of direct gaze may be more efficient (Reddy and Kanwisher, 2006). Such efficient coding would be associated with less metabolic cost and therefore lower neural responses facilitating its access to awareness at lower neural thresholds.

Eye movements towards unconscious fear-conditioned stimuli

The aim of Study 3 was to investigate whether attentional biases similar to that observed for eye contact (Study 1) can be observed for fear-conditioned stimuli suppressed from awareness. While eye contact is an inherently salient, social stimulus, fear-conditioning ascribes salience to a previously neutral stimulus. The fear-conditioning procedure was effective in changing participants' subjective affect to the stimuli and in increasing participants' arousal. However, eye movements were not biased towards the fear-conditioned stimulus when it was suppressed from awareness. Several factors could be responsible for the results obtained in Study 3. Although previous studies have observed physiological responses to unconscious fear-conditioned stimuli (review: Dimberg and Öhman, 1996), these studies have been criticized for not adequately assessing awareness (Lovibond and Shanks, 2002; Pessoa, 2005). In fact, SCRs to conditioned stimuli depend on the extent to which these stimuli are suppressed from awareness, with higher conditioned responses to stimuli that are less suppressed (Cornwell et al., 2007). Thus, attentional biases to fear-conditioned stimuli might depend on awareness. In a like manner, fear-conditioned stimuli presented outside of awareness might only have an influence at the physiological level (Raio et al., 2012) and other behaviour-relevant functions like eye movements are not influenced. Another explanation could be that fearful faces, the stimulus material used in our study, may have itself biased attention and masked any subtle effects of conditioning. However, the fear-conditioning procedure is well established with fearful faces (Öhman and Mineka, 2001), which are less prone to extinction effects, a factor that was critical for the study. Preliminary evidence suggesting that oculomotor biases towards conditioned stimuli might be dependent on the strength of the conditioned response could also explain the overall absence of a bias to the CS+ stimulus at the group-level. In other words, a sufficiently high level of physiological arousal might be required for eye movement biases towards fear-conditioned stimuli.

Summary and Outlook

Taken together, the studies show that inherently socially salient stimuli can be processed outside of awareness, influence ongoing behaviour and that their neural processing is more efficient compared to other stimuli. In particular, the preliminary results showing an unconscious eye gaze avoidance in ASD in comparison to the unconscious preference for direct gaze in TD adults (Study 1) offer a starting point for the development of new diagnostic and intervention techniques in autism. For example, the neural responses to eye gaze in infants are a predictor for the later development of autism (Elsabbagh et al., 2012). Similarly, the extent to which unconscious eye avoidance could be predictive of the later development of autistic-like traits is a question for future research. Moreover, the neural mechanism reported in Study 2 for the privileged processing of direct eye gaze may well generalize to other domains, e.g., other stimuli that are of high ecological relevance. Whether similar mechanisms exist for other ecologically relevant stimuli is an empirical question that is to be investigated.

An interesting question that arises from the current thesis is why a saccadic bias was observed for eye gaze but not for fear-conditioned stimuli. There are several reasons that could have contributed to the observed results. Firstly, in Studies 1 and 2 only the direction of eye gaze, a single feature, differed between the stimuli. In contrast, in Study 3, through fear conditioning aversiveness was ascribed to the entire face stimulus. Thus a saccadic bias to the fear-conditioned CS+ face would hinge on face identity processing, a more complex process than the processing of a single feature. This strongly suggests that intact configural face processing under interocular suppression affects eye movements while holistic face processing is impaired under CFS. Indeed, it has recently been discussed that awareness might be required for holistic face processing, an essential component of face recognition (Axelrod et al., 2015). Thus, follow up experiments could investigate saccadic biases to fear-conditioned stimuli where only a single feature is conditioned. In fact, fear-conditioned stimuli, in which a single stimulus feature is conditioned (for example, colour), access awareness faster than neutral stimuli (Gayet et al., 2016). Although this study measured the access to awareness, which, as mentioned in the introduction, does not equal unconscious processing (Stein and Sterzer, 2014), it lends support to the idea that unconscious biases might be observed for low-level conditioned stimuli. A second reason for the discrepant results of Studies 1 and 3 could be due to the value or salience of the stimulus itself. Eye gaze is a feature that is inherently salient, whereas a fear-conditioned stimulus acquires salience. Thus, unconscious attentional biases at the level of eye movements might depend on the strength of the salience. In line with this notion, saccadic biases to the CS+ stimulus correlated with the arousal evoked in participants (see results of Study 3).

In summary, the results of all four studies greatly expand our understanding of the processing of socially relevant stimuli in the human visual system, while contributing to the long standing discussion on the extent to which high level information can be processed outside awareness (Kouider and Dehaene, 2007). Finally, they provide a platform for future research in both typically developed and psychiatric populations.

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7 Affidavit

I, Apoorva Rajiv Madipakkam, certify under penalty of perjury by my own signature that I have submitted the thesis on the topic, “*The conscious and unconscious processing of socially relevant visual stimuli*”. I wrote this thesis independently and without assistance from third parties, I used no other aids than the listed sources and resources.

All points based literally or in spirit on publications or presentations of other authors are, as such, in proper citations (see "uniform requirements for manuscripts (URM)" the ICMJE www.icmje.org) indicated. The sections on methodology (in particular practical work, laboratory requirements, statistical processing) and results (in particular images, graphics and tables) correspond to the URM (s.o) and are answered by me. My contributions in the selected publications for this dissertation correspond to those that are specified in the following joint declaration with the responsible person and supervisor. All publications resulting from this thesis and which I am author of correspond to the URM (see above) and I am solely responsible.

The importance of this affidavit and the criminal consequences of a false affidavit (section 156,161 of the Criminal Code) are known to me and I understand the rights and responsibilities stated therein.

Date Signature

Declaration of any eventual publications

Apoorva Rajiv Madipakkam had the following share in the following publications:

Published peer-reviewed articles:

1) Rothkirch M*, **Madipakkam AR***, Rehn E, Sterzer P. Making Eye Contact Without Awareness. *Cognition*, 2015, 143:108-114. (* equal contribution)

   45%

   Contributions in detail:
   - Programming the experiment in Matlab
   - Recruiting and collecting eye movement recordings from participants
   - Statistical analysis of data with independently written scripts in Matlab
   - Revision of the manuscript

2) **Madipakkam AR**, Rothkirch M, Guggenmos M, Heinz A, Sterzer P. Gaze Direction Modulates the Relation between Neural Responses to Faces and Visual Awareness. *Journal of Neuroscience,* 2015, 35(39):13287-99.

   75%

   Contributions in detail:
   - Programming the experiment in Matlab
   - Recruiting and testing participants in the fMRI scanner
   - Statistical analysis of data with independently written scripts in Matlab
   - Writing the first version of the manuscript
   - Submission and subsequent revisions of the manuscript

3) **Madipakkam AR**, Rothkirch M, Wilbertz G, Sterzer P. Probing the Influence of Unconscious Fear-Conditioned Visual Stimuli on Eye Movements. *Consciousness and Cognition*, 2016, 46:60-70

   80%

   Contributions in detail:
   - Programming the experiment in Matlab
   - Recruiting and collecting eye movement recordings and skin conductance data from participants

- Statistical analysis of data in Matlab
- Writing the first version of the manuscript
- Submission and subsequent revisions of the manuscript

Signature, date and stamp of the supervising University teacher

Signature of the doctoral candidate

8 Printouts of the Publications

1) Rothkirch M*, **Madipakkam AR***, Rehn E, Sterzer P. Making Eye Contact Without Awareness. *Cognition*, 2015, 143:108-114. (* equal contribution)
DOI: https://doi.org/10.1016/j.cognition.2015.06.012
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3) **Madipakkam AR**, Rothkirch M, Wilbertz G, Sterzer P. Probing the Influence of Unconscious Fear-Conditioned Visual Stimuli on Eye Movements. *Consciousness and Cognition*, 2016, 46:60-70
DOI: https://doi.org/10.1016/j.concog.2016.09.016
Impact Factor: 2.18

9 Curriculum Vitae

Mein Lebenslauf wird aus datenschutzrechtlichen Gründen in der elektronischen Version meiner Arbeit nicht veröffentlicht.

My CV will not be published in the electronic version of my PhD thesis due to data privacy.

10 Complete Publication list

Published original articles

Madipakkam AR, Rothkirch M, Wilbertz G, Sterzer P. Probing the Influence of Unconscious Fear-Conditioned Visual Stimuli on Eye Movements. *Consciousness and Cognition*, 2016, 46:60-70

Shen C, Velenosi L, **Madipakkam AR**, Edemann HC, Stasch J, Neuhaus AH. Influence of Time Course and Identity on N170 Adaptation. *Cortex*, 2016, 86:55-63

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Rothkirch M*, **Madipakkam AR***, Rehn E, Sterzer P. Making Eye Contact Without Awareness. *Cognition*, 2015, 143:108-114. (*equal contribution)

Madipakkam AR, Ludwig K, Rothkirch M, Hesselmann G. Now You See it, Now You Don't: Interacting With Invisible Objects. *Frontiers for Young Minds,* 2015, 3:4.

Articles in preparation

Madipakkam AR, Rothkirch M, Dziobek I, Sterzer P (in preparation). Unconscious Eye Avoidance in Autism Spectrum Disorder

Madipakkam AR, Rothkirch M, Dziobek I, Sterzer P (in preparation). Access to awareness of direct gaze is related to autistic traits

Conference Contributions

Talks

August 2015 — **Madipakkam AR**, Rothkirch M, Guggenmos M, Heinz A, Sterzer P

The processing of socially relevant stimuli in relation to visual awareness

14th Charité Conference in Psychiatric Research: Emotional Neuroscience, Berlin, Germany

May 2014 — **Madipakkam AR**, Rothkirch M, Rehn E, Sterzer P

Making Eye contact without awareness

Vision Sciences Society (VSS), 14th Annual Symposium, Florida

Posters

August 2016 — **Madipakkam AR**, Rothkirch M, Kelly K, Wilbertz G, Sterzer P

Effect of unconscious fear-conditioned stimuli on eye movements

39th European Conference on Visual Perception (ECVP), Barcelona

March 2016 — **Madipakkam AR**, Rothkirch M, Dziobek I, Sterzer P

Oculomotor bias to unconsciously presented faces with direct gaze is absent in autism spectrum disorder

9th Scientific Meeting for Autism Spectrum Conditions, Freiburg

September 2014 — **Madipakkam AR**, Rothkirch M, Rehn E, Sterzer P

Making Eye contact without awareness

European Summer School on Eye Movements (ESSEM), Freiburg

June 2014 — **Madipakkam AR**, Rothkirch M, Guggenmos M, Sterzer P

The neural correlates of conscious and unconscious gaze processing

20th Annual Meeting of the Organization for Human Brain Mapping, Hamburg

May 2014 — Rothkirch M, **Madipakkam AR**, Sterzer P

Unconscious processing of eye gaze direction in the human brain

Vision Sciences Society (VSS), 14th Annual Symposium, Florida

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