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Threat and trait anxiety affect stability of gaze fixation

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ABSTRACT

Threat accelerates early visual information processing, as shown by shorter P100 latencies of pattern Visual Evoked Potentials in subjects with low trait anxiety, but the opposite is true for high anxious subjects. We sought to determine if, and how, threat and trait anxiety interact to affect stability of gaze fixation. We used video oculography to record gaze position in the presence and in the absence of a fixational stimulus, in a safe and a verbal threat condition in subjects characterised for their trait anxiety. Trait anxiety significantly predicted fixational instability in the threat condition. An extreme tertile analysis revealed that fixation was less stable in the high anxiety group, especially under threat or in the absence of a stimulus. The effects of anxiety extend to perceptual and sensorimotor processes. These results have implications for the understanding of individual differences in occulomotor planning and visually guided behavior.

1. Introduction

One of the primary roles of the gaze system is to bring and hold visual stimuli of interest onto the fovea, the central area of human retina showing the highest visual acuity, necessary for post-retinal processing. Even during fixation on a stationary stimulus/object (visually guided fixation), constant, small, involuntary "microsaccadic" eye movements prevent the naturally occurring adaptation of post-retinal cortical cellular mechanisms (Movshon and Lennie, 1979; Webster and De Valois, 1985), which would otherwise lead to depression of sensitivity/salience and even fading of a visual target following prolonged stabilisation of its image on the fovea (Troxler, 1804; Blakemore and Campbell, 1969). Apart from preventing retinal fading of a visual target, microsaccades also serve to bring the line of sight to visual details that are crucial for finely guided visuomotor tasks that require the highest level of spatial resolution (Steinman et al., 1973; Ko et al., 2010). Yet, in addition to improve spatial resolution, microsaccades are thought to transform the visual scene into a sequence of discrete views which, one at a time, are processed by attentional resources and guide decision making (Ballard et al., 1997; Ko et al., 2010; Kowler and Collewijn, 2010). Microsaccades may thus be prompted by cognition and reflect attentional processing and fine strategic visuomotor planning.

Initiation of visually triggered microsaccades involves occipital and parietal cortical inputs, including retinal input to "fixation neurons" in the superior colliculus, which then projects to the premotor circuit in the brain stem and cerebellum (Munoz and Istvan, 1998; Munoz and Wurtz, 1993a,b). Suppression of reflexive microsaccades is under the tonic control of frontal cortex and basal ganglia, which also project to the superior colliculus and brain stem premotor circuit (Hikosaka et al., 2000; Munoz et al., 2000; Schall, 1997 for review). Fixation in the absence of a visual stimulus (volitional fixation) is less accurate than stimulus-driven fixation (Smyrnis et al., 2003) and may be driven almost entirely by extra-retinal, prefrontal/basal ganglia input to the SC fixation neurons (Munoz and Wurtz, 1993a; Hikosaka et al., 2000; Munoz et al., 2000; Schall, 1997 for review). It has been hypothesized (Smyrnis et al., 2004) that these prefrontal regions maintain a "mental" representation of the fixation point and thus may be the same areas mediating spatial memory processing (Goldman-Rakic, 1988). Indeed, it is well-established that a particular region of the frontal lobe neocortex, the frontal eye field (FEF) is prominently involved in control of volitional eye movements, having a distinct sub-region for fixation. The dorsolateral prefrontal cortex in particular, acts as a ≪supervisory≫ area, inhibiting unwanted reflexive saccades when volitional maintenance of fixation is required (Gooding, 1999).

Suppression of microsaccades results in stable fixation such as that seen in trained athletes e.g. elite shooters and has been related to their superiority in selective and sustained attention (Di Russo et al., 2003). On the other hand, deficient fixational stability is

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seen in conditions characterised by attentional and strategic planning deficits due to fronto-striatal pathology, such as schizophrenia (Burton et al., 2008) and attention-deficit hyperactivity disorder (ADHD) (Munoz et al., 2003). Trait anxiety is associated with impoverished recruitment of attentional control mechanisms (Fox, 1993; Eysenck and Calvo, 1992; Bishop, 2009) and for this reason it is expected to impact on reflexive and volitional saccadic control. Threat commands visual attention through activation of the amygdala and the bed nucleus of stria terminalis (Lang et al., 2000) and is thus preferentially detected in humans (Ohman et al., 2001); it adaptively enhances contrast perception (Phelps et al., 2006) and accelerates the early P100 wave of pattern Visual Evoked Potentials (Laretzaki et al., 2010). The latter effect however, was not observed in high trait anxiety subjects (Laretzaki et al., 2010). This was probably a result of a hyper-responsive pre-attentive, amygdala-centred threat-detection system (Mathews et al., 1997), associated with deficient recruitment of prefrontal cortical mechanisms that are critical in the top–down control of selective attention to threat (Bishop et al., 2004; Ohman, 2005).

In the present study, we sought to determine if, and how, threat and trait anxiety interact to affect fixation of gaze. To this goal, we studied the effects of verbal threat on stimulus driven (a non-emotional target) and volitional (no-target, empty screen) fixation performance, in healthy subjects characterised for their trait anxiety. Subjects were also tested in the absence of threat. Based on available evidence, we predicted generally better fixation performance in the stimulus driven compared to volitional fixation condition. We also predicted that threat would impair fixation performance especially in high trait anxious subjects and this impairment would be more pronounced under volitional fixation since the latter is more critically determined by prefrontal input in the SC. Because of inadequate data in the literature, we made no predictions regarding group differences (high vs. low trait anxious subjects) in fixation performance in the absence of threat.

2. Materials and methods

2.1. Subjects

This study was conducted in compliance with the declaration of Helsinki and followed a protocol approved by the Ethics Committee of the University of Crete, and all participants gave their written informed consent. Participants ($n = 44$, age: 26 ± 5 yrs) were randomly recruited by phone from a pool of 560 healthy male volunteers, characterised for trait anxiety (median trait anxiety score: 36, mean: 36.45, range: 20–68), with the widely accepted State-Trait Anxiety Inventory (STAI-T) (Spielberger, 1983). Care was taken that the present sample was representative of the large cohort (20 were above and 24 below the cohort's median) covering the entire range of the cohort's STAI-T values. These volunteers had previously undergone thorough psychiatric and medical assessment including drug screening and they were free from history or presence of head trauma, medical neurological and psychiatric conditions, including use of prescribed or recreational drugs. Additional criteria for inclusion in the present study were absence of ocular or corneal disease, normal binocular and colour vision and optical correction (if needed) with spectacles for the viewing distance. Recruited subjects underwent an ophthalmological examination and a new urine drug screening test. Participants were tested between 9:00 am and 4:00 pm in one session.

2.2. Eye tracking

Fixational gaze movements from both eyes were recorded simultaneously using video oculography (EyeLink II, SR Research Ltd., Canada). Eyelink II consists of two miniature head-mounted infrared cameras that record eye position using pupil or pupil-cornea tracking. A third camera monitors subjects' head position relative to four infrared markers mounted on the display screen. According to the manufacturer, Eyelink II has a spatial resolution higher than 0.01° for two-dimensional eye tracking. In this study horizontal and vertical eye positions were recorded using the pupil-cornea tracking mode at a sample rate of 250 Hz. All measurements were performed with subjects seated on a chair and with their head stabilised by means of a chin rest to minimise head movements. A system calibration/validation was performed every time prior to recording to correlate the output results.

2.3. Subjective measures

The subjects' moods and feelings were self-rated on a 16-item visual analogue scales (VAS – see Supplemental file) originally developed for measuring drug-induced changes in mood and alertness (Aitken, 1969; Norris, 1971). Subsequently, these scales were found to be very sensitive to momentary changes in psychological states caused by psychological manipulations such as verbal threat (Bitsios et al., 1996, 1998a,b). They are easy and much faster (<60 s) to score than the Spielberger's State anxiety scale, they measure short term changes in anxiety and they are able to distinguish between changes in arousal levels and the emotion of anxiety. This is important as it has been shown previously that arousal may increase without accompanying increases in anxiety (Bitsios et al., 2004). The raw values (mm) for each item and each subject were weighted by multiplication with their respective factor loading and the weighted values for each item and subject were then allocated to 'alertness' (9 items), 'discontentment' (5 items) and 'anxiety' (2 items) factors, based on a principal component analysis (Bond and Lader, 1974). The average of the weighted group values for each factor was entered in the statistical analysis.

2.4. Part 1: testing procedure and training

Subjects had been previously informed that they would participate in one session where their fixational stability would be tested under various psychological conditions relevant to anxiety research. On arrival to the lab, all participants rested for 5 min during which they self rated their anxiety, alertness and mood using Visual Analogue Scale (VAS) questionnaires. Eye dominancy was determined by looking through a central hole in an A4 card, held by the participant in both hands away from the body. Subsequently, eye position data were obtained binocularly for two viewing conditions which were counterbalanced between subjects: in the absence of a fixational stimulus (volitional fixation), in which the volunteer was asked to keep fixation at the centre of the screen, and in the presence of a fixational stimulus (stimulus-driven fixation).

The stimulus, presented on a 21″ Sony GDM F-520 CRT monitor, was generated using custom written software for a VSG 2/5 stimulus generator card (Cambridge Research Systems Ltd., UK). The monitor was viewed from a distance of 100 cm. The stimulus was a 'profiled' spot, having a radial symmetrical spatial configuration of a blurred disk with a 0.25° flat top and a raised cosinusoidal skirt of 0.5° in diameter. The stimulus was presented at a Weber contrast of 40% for a total period of 15 s. The surround had a luminance (L) of 30 cd/m^2 (chromatic co-ordinates: $x = 0.310$, $y = 0.316$).

Recordings in this part served as 'training' in order to reduce novelty related arousal and familiarise subjects with the experimental procedures and were thus discarded from further analysis. At the end of part 1, subjects rated themselves again with the VAS, which was considered to be a more reliable baseline, since it was not confounded by novelty related arousal. Following these training procedures in part 1, subjects were given detailed instructions (see below) for part 2. They were reminded that they did not have to participate any further, however, all subjects agreed to participate and signed new consent forms for part 2 of the session.

2.5. Part 2: main session

The two viewing conditions described above were repeated with the same within-subject order as in training, under two psychological periods: they were both identical to training in part 1 but one was under verbal threat ("threat" period) and the other was not ("safe" period). Our verbal threat protocol has been described in detail previously (Bitsios et al., 2002, 1996; Hourdaki et al., 2005; Laretzaki et al., 2010). Briefly here, verbal threat (of electrical shock) was induced throughout the "threat" periods, by the presence of a Grass stimulator (SD 9) connected to the skin overlying the median nerve of the left wrist through disposable silver surface electrodes. Before and after connection to wrist electrodes, subjects completed the VAS questionnaires (see Fig. 1), in order to test whether electrode connection, a powerful contextual threat stimulus (Baas et al., 2002), induced adequate levels of anxiety. Subjects had been instructed to anticipate a total of 1–3 electric shocks but they were not aware of the exact number and timing of the electric shock(s). These were described as painful stimuli inducing a short-lived localized unpleasant sensation on the wrist. As threat was the actual variable of interest, no electric shock was actually delivered.

Half of the subjects within each trait anxiety group started with the "safe" and the other half with the "threat" condition. Therefore, there were four conditions (safe/volitional fixation, safe/stimulus driven fixation, threat/volitional fixation and threat/stimulus driven fixation) within each subject, which were all counterbalanced between subjects.

2.6. Data reduction and analysis

Data analysis was performed offline using custom-made scripts written in computational software (Matlab vs. 7.6.0.324). Fixation performance was evaluated using the Bivariate Ellipse Contour Area (BCEA), a mathematical description of fixation stability (Steinman, 1965). If the measured gaze positions are assumed to have a bivariate normal distribution, the ellipse area (BCEA) can be calculated using Eq. (1), where σ_H and σ_V are the standard deviations of position over the horizontal (x)