Face Perception in Social Anxiety: Visuocortical Dynamics Reveal Propensities for Hypervigilance or Avoidance

Supplemental Information

Supplemental Methods

CGI severity ratings (1) were determined with the following guidelines.

CGI – Severity of Illness Rating Guidelines

1 NORMAL - No anxiety/fear in excess of normal. No avoidance or impairment. May still become somewhat anxious/ fearful under certain circumstances (e.g., before an important event), but anxiety/fear is not persistent.
2 MINIMALLY ILL - Some anxiety/fear in excess of normal, but rare avoidance or significant distress. No clear impairment in functioning and no more than normal concern about having the anxiety/fear.
3 MILDLY ILL - Almost meets criteria for a diagnosis, but phobic situations are not regularly avoided or endured with intense anxiety; *OR* there is only minimal impairment in functioning and no marked distress about having the fear.
4 MODERATELY ILL - Modest kinds of impairment (i.e. discomfort but no significant disruptions in important areas of functioning (e.g., social, work area). However, there are clear episodes of marked anxiety/fear.
5 MARKED ILLNESS - Significant impairment in important areas of functioning but not gross impairment. The patient can hold a reasonably decent job and have some social activities that are fairly comfortable although there are limitations in both areas.
6 SEVERE ILLNESS - The patient might be severely impaired in several areas of functioning (e.g., work, social activities) OR totally impaired in one but less in other activities. A reasonable observer would see severe problems in functioning in these individuals.
7 AMONG THE MOST SEVERELY ILL PATIENTS - The patient is totally disabled.

Normative Ratings of Facial Expressions

Ninety-six pictures were selected from the Karolinska Directed Emotional Faces (KDEF (2) http://www.facialstimuli.com/) of 24 actors gazing directly at the viewer (12 female, 12 male actors) posing 4 different expressions (neutral, happy, fearful, angry),

in front of a gray background. For comparison with prior face-processing (3) studies as well as ssVEP investigations of emotional scenes (4), an online pilot study was conducted to gather normative affective ratings of the 96 stimuli selected for the laboratory session. This study allowed us to collect complementary evidence as to whether or not the face stimuli conveyed the intended expression and in turn elicited a reliable affective response in viewers. This was especially important given the lack of differentiation among facial expression in ssVEP amplitude in all groups except the circumscribed social anxiety patients. The rating study also aimed to inform the present study regarding potential stimulus differences in emotional intensity, known to affect the ssVEP. For course credit 242 students (mean age=18.37; SD=0.85; 73% female) from undergraduate psychology courses provided informed consent and then viewed and rated pseudorandom presentations of each facial expression with the Self-Assessment Manikin (SAM) (5) to assess three dimensions: experienced pleasure, emotional arousal, and dominance. A subset of this normative data (n=140) was previously published (6). Additional participants were recruited and these results represent the full sample (n=242). See Supplemental Table S1 for means and standard deviations. Repeated measures ANOVAs were performed separately on these dimensions with facial expression as the within-subjects factor. Arousal varied across expressions, $F(3,723)=102.57$, $p<.001$, with the most intense ratings for angry, followed by fearful, happy, and lastly neutral. The mean arousal for all expression pairs reliably differed, contrasts $Fs=12.61\text{-}260.22$, $ps<.001$, except for the two most arousing conditions, fearful versus angry, *ns*. Expression also influenced hedonic valence, $F(3,723)=909.26$, $p<.001$, with the most aversion reported for angry, followed by fearful, and the most

pleasure for happy expressions. Similar to rated arousal, the mean pleasure for all expressions reliably differed, contrasts *Fs*=72.82-1358.28, *ps*<.001. Expression also influenced subjective sense of control, $F(3,723)=10.15$, $p<.001$ with the lowest ratings of control or agency related to viewing fearful, followed by angry, neutral, and lastly happy expressions, with all expression pairs differing except neutral and angry, *Fs*=5.56-17.40, *ps*<.001. Notably, the ratings are within the range typically observed for neutral and low arousing International Affective Picture System (IAPS; 7), and are far less arousing that those used in studies with reliable affective modulation of the ssVEP.

Supplemental Table S1. Normative pleasure, arousal and dominance ratings (N=242) of KDEF stimuli on Self-Assessment Manikin (SAM) by expression

Facial Expression	Pleasure	Arousal	Dominance
Neutral	4.67 (0.52)	3.56 (1.32)	5.24 (1.35)
Happy	7.15 (0.96)	4.57 (1.73)	5.45 (1.77)
Fearful	3.75 (1.06)	4.95 (1.46)	4.89 (1.41)
Angry	3.42 (1.14)	5.02 (1.48)	5.09 (1.46)

Note. Pleasure rated on SAM (5): 1=Completely unhappy, 9=Completely happy; Arousal: 1=Completely relaxed, 9=Completely aroused; Dominance 1=Completely dominant, 9=Completely submissive.

EEG Data Processing and ssVEP Internal Reliability

Based on the distributions of absolute voltage, standard deviation, and maximum of the first temporal derivate, channel-specific artifacts were first detected using the recording reference (i.e., Cz), and then global artifacts were detected using a mathematically derived average reference (8). The Cz reference was used for recording only, and the average reference was calculated after artifact rejection and used for all subsequent analyses. Sensors that were contaminated throughout were replaced with a statistically weighted spherical spline interpolation from the full channel set (median of 5 channels in this study), and individual trials were rejected when more than 17 channels

were identified as bad (8). Note that Oz was never interpolated across the experiment. No eye movement correction was applied. After artifact rejection, an average of 17.6 trials/condition was retained in the analyses, with averages not differing between expressions (happy: 16.8; neutral: 18.1; fearful: 17.9; angry: 17.7).

Regarding internal consistency of the ssVEP measures, we calculated Cronbach's coefficient alpha of the mean occipital ssVEP amplitude evoked by the 4 expressions, which was 0.96 (excellent internal consistency). More importantly, the differences in ssVEP amplitude between neutral and each emotional expression (a more interesting and germane metric of how reliable emotional expression-related ssVEP differences occur across participants) reached a Cronbach's coefficient of 0.68, which is considered high internal consistency.

Supplemental Results

Subjective Symptom Patterns and Principal Diagnosis

The pattern of electrocortical enhancement to aversive expressions specific to circumscribed social anxiety was not explained by self-reported symptoms putatively more specific to social anxiety versus panic disorder or by transdiagnostic broad negative affectivity or functional interference (Table 2). That is, social fear and avoidance (Liebowitz Social Anxiety Scale-Self-report, LSAS-SR (9); Fear Survey Schedule, FSS Social Subscale (10)) reliably increased from control participants to circumscribed social anxiety, PDA and generalized social anxiety patients far more elevated than all groups. Notably, circumscribed social anxiety and PDA reported similarly moderate levels of social fear and avoidance. Panic related-distress was most

elevated in PDA followed by generalized, then circumscribed social anxiety and normative levels among control participants. This pattern emerged in panic attack frequency and severity (Panic Disorder Severity Scale, PDSS, (11)) interoceptive hyperarousal (Anxiety Sensitivity Index, ASI (12), Mood and Anxiety Symptom Questionnaire, MASQ Anxious Arousal (13)), and agoraphobic situational fearfulness (FSS Agoraphobia subscale). Measures assessing non-specific affective distress or broad negative affectivity reliably increased from control participants to circumscribed social anxiety, PDA and generalized social anxiety patients at the extreme. More, specifically, this was evident in non-specific anxiety (State-Trait Anxiety Inventory, STAI (14); MASQ General Anxiety) and depression (MASQ General Depression) and their shared symptoms (MASQ Mixed Symptoms), cognitive and somatic depressive symptoms (Beck Depression Inventory-II, BDI-II (15)), anhedonia (MASQ Anhedonia), and rumination and worry (Penn State Worry Questionnaire, PSWQ (16)).

Transdiagnostic functional impairment (Illness Intrusiveness Ratings Scale, IIRS (17)) indicated similarly substantial illness intrusiveness among generalized social anxiety and PDA patients relative to modest intrusiveness in daily functioning for circumscribed social anxiety patients. For an index of transdiagnostic clinical global impression of severity, the 28 CGI-S ratings of Axis I and II disorders made by the interviewers for each participant were summed for a single composite, which showed the same pattern (Table 2). Potentially reflective of disorder-related impairment in educational situations, the percent of each group that attained a college degree or beyond showed the same pattern. In terms of clinician ratings, treatment prognosis aligned with broad negative affectivity—worst for generalized social anxiety followed by

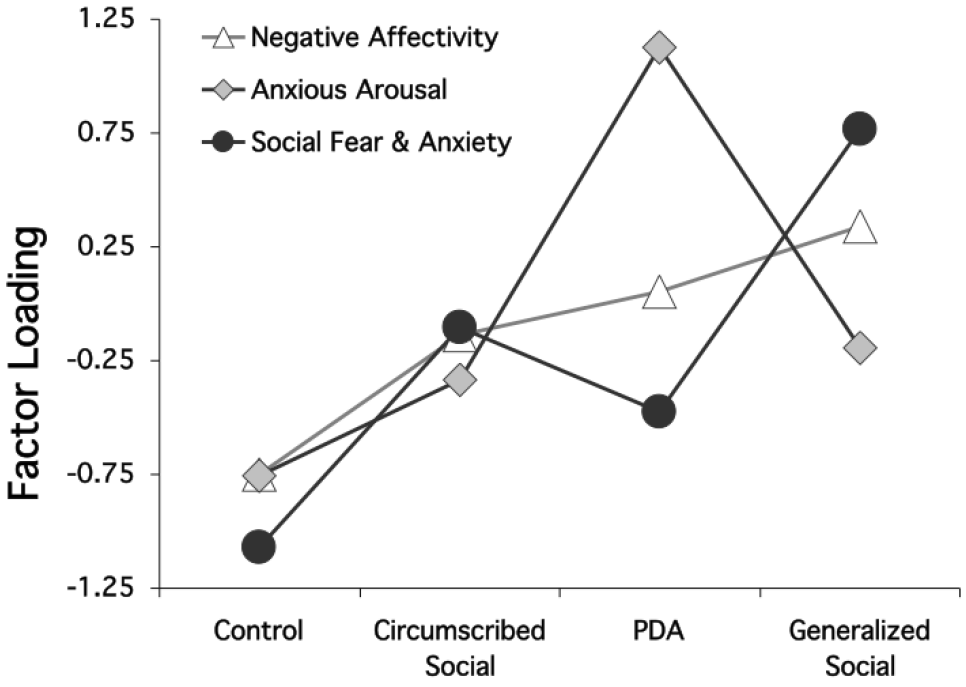
PDA and then circumscribed social anxiety patients predicted to fair best. In contrast, clinical global impressions of severity (CGI-S) ratings by disorder reflected elevations specific to the respective principal disorder—ratings for social anxiety highest for its subtypes (worst for generalized social anxiety) while panic disorder and agoraphobia were rated most severe for PDA. Furthermore, neither medication usage (see following materials), diagnostic comorbidity (Table 2), or demographics (Table 2) appeared to systematically modulate the ssVEP.

To meaningfully reduce the array of questionnaires to underlying dimensions, we conducted a principal components analysis using the dimensional symptom measures. Following varimax rotation (based on three unrotated factors), the analysis resulted in three factors of: 1) general distress/negative affectivity ($\lambda = 8.91$), which accounted for the most variance (59.37%), 2) anxious/hyperarousal ($\lambda = 1.82$; 12.12% of variance), and 3) social fear and anxiety ($\lambda = 0.86$, 5.73% of variance). The following table lists the factor loadings for individual questionnaires, which were consistently high (0.54-0.86) and showed clear single-component loading with the exception of the nearly equivalent cross-loadings for the Illness Intrusiveness Rating Scale (i.e., 0.39-0.54) across all factors and the equivalent loadings on components one and three for the Penn State Worry Questionnaire (i.e., 0.57-0.58). The questionnaires also loaded onto specific factors in a manner largely consistent with discriminable face validity.

Supplemental Table S2. Varimax-Rotated Factor Loadings of Questionnaires Across Participants (N=105)

Scale/Subscale Total	*Component 1: Negative Affectivity*	*Component 2: Anxious Arousal*	*Component 3: Social Fear*
LSAS Total	0.40	0.19	**0.77**
FSS Social Fears	0.33	0.15	**0.84**
FSS Agoraphobia	-.04	**0.76**	0.37
Panic Disorder Severity Scale	0.24	**0.73**	0.24
Anxiety Sensitivity	0.27	**0.86**	0.15
MASQ: Anxious Arousal	0.40	**0.72**	-0.02
MASQ: General Anxiety	0.40	**0.59**	0.13
MASQ: Mixed Symptoms	**0.82**	0.29	0.22
MASQ: General Depression	**0.82**	0.15	0.39
MASQ: Anhedonia	**0.80**	0.20	0.32
Beck Depression Inventory-II	**0.70**	0.32	0.38
STAI: Trait Anxiety	**0.72**	0.32	0.51
Penn State Worry	0.57	0.26	.058
Illness Intrusiveness	.39	0.51	0.54

Note. LSAS= Liebowitz Social Anxiety Scale (9); FSS=Fear Survey Schedule (10); MASQ=Mood and Anxiety Symptom Questionnaire (13); BDI-II=Beck Depression Inventory-II (15); STAI= State-Trait Anxiety Inventory (14).

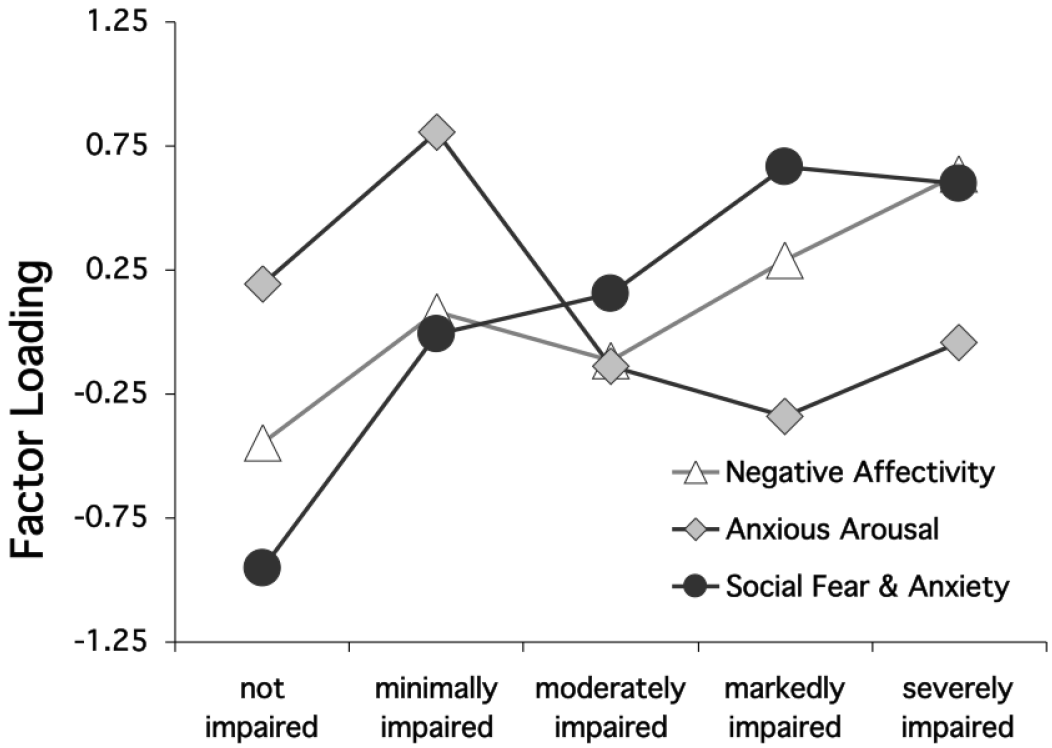


Supplemental Figure S1. Mean factor loadings by principal disorder resulting from a principal components analysis across the dimensional symptom measures in Table 2, which yielded factors of general negative affectivity, anxious arousal, and social fear/avoidance. Control (N=17); Circumscribed social anxiety (N=21); Generalized Social anxiety (N=42); PDA=Panic disorder with agoraphobia (N=25).

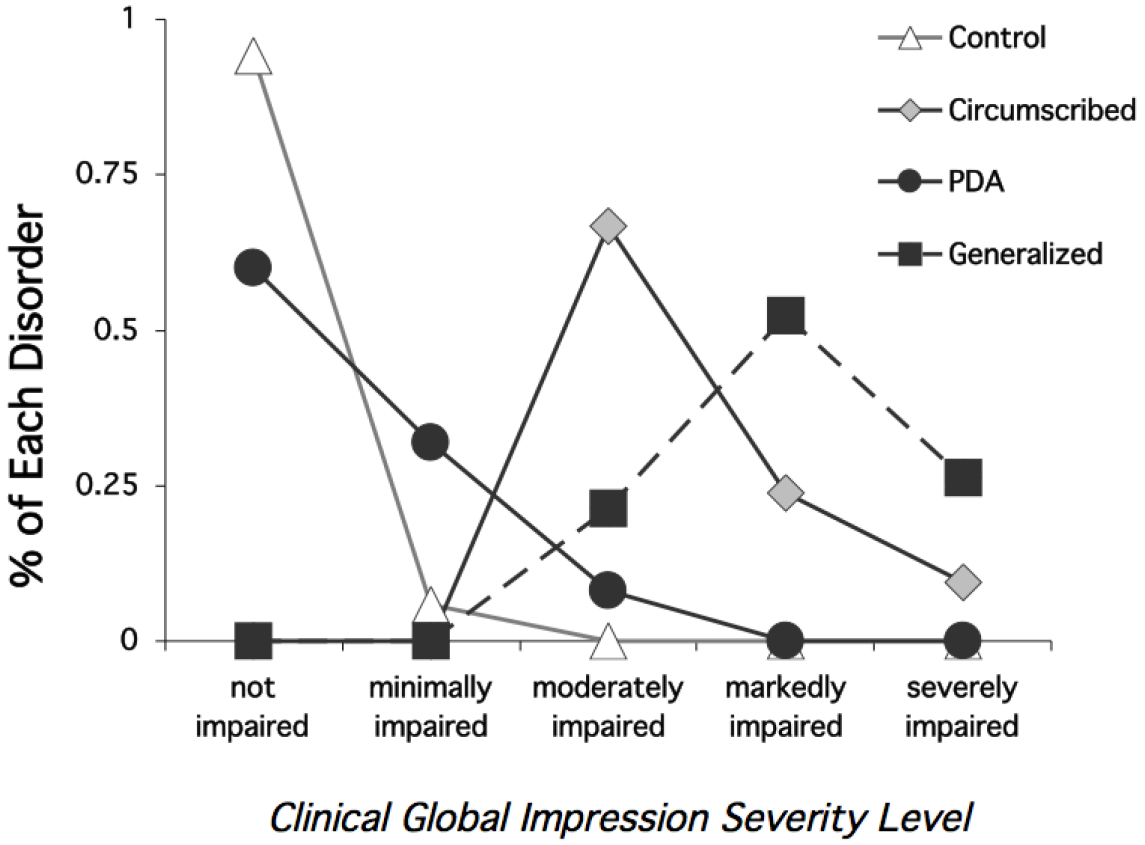
Medication and Drug Use

Medication usage did not reliably differ among patient groups, considering all medications (circumscribed social (42.9%; n=9), PDA (36%; n=9), generalized social (40.5%; n=17), Group, $X^2(2)=.24$, *ns*) or individual classes. Accounting for medication in the omnibus model showed no influence or interactions on ssVEP modulation or amplitude and the interaction of group and expression remained. The low rates of usage of individual drug classes largely precluded meaningful statistical analysis but in the interest of completeness sample proportions and group comparisons for the most frequently endorsed psychotropics by medication and principal disorder follow. Benzodiazepines: circumscribed social (19%; n=4), PDA (20%; n=5), generalized social (19%; n=8), Group, $X^2(2)=.01$, *ns*; Selective serotonin reuptake inhibitors: circumscribed social (13.4%; n=3), PDA (12%; n=3), generalized social (14.3%; n=6), Group, $X^2(2)=.079$, *ns*; Norepinephrine-dopamine reuptake inhibitors: circumscribed social (0%), PDA (4%; n=1), generalized social (9.5%; n=4), Group, $X^2(2)=2.55$, *ns*; Stimulant: circumscribed social (9.5%; n=2), PDA (0%), generalized social (9.5%; n=4), Group, $X^2(2)=2.56$, *ns*; Non-benzodiazepine hypnotic: circumscribed social (9.5%; n=2), PDA (4%; n=1), generalized social (2.4%; n=1), Group, $X^2(2)=1.67$, *ns*; Atypical antipsychotic: circumscribed social (0%), PDA (0%), generalized social (7.1%; n=3), Group, $X^2(2)=3.40$, *ns*; Mood stabilizer/anticonvulsant: circumscribed social (4.8%; n=1), PDA (4%; n=1), generalized social (0%), Group, $X^2(2)=1.90$, *ns*; Serotonin-norepinephrine reuptake inhibitors: circumscribed social (0%), PDA (0%), generalized social (2.4%; n=1), Group, $X^2(2)=1.12$, *ns*; Noradrenergic and specific serotonergic antidepressant: circumscribed social (0%), PDA (0%), generalized social (2.4%; n=1),

Group, $X^2(2)=1.11$, *ns*; Tricyclic antidepressant: circumscribed social (0%), PDA (4%; n=1), generalized social (0%), Group, $X^2(2)=2.55$, *ns*; Serotonin 5-HT1A receptor partial agonist: circumscribed social (0%), PDA (0%), generalized social (2.4%; n=1), Group, $X^2(2)=1.11$, *ns*; Beta-blocker: circumscribed social (0%), PDA (4%; n=1), generalized social (0%), Group, $X^2(2)=2.55$, *ns*. Furthermore, groups did not differ in rates of current cigarette smoking, circumscribed social (0%), PDA (0%), generalized social (2.4%; n=1), Group, $X^2(2)=1.11$, *ns*.



Supplemental Figure S2. Factor loading on the three factors resulting from principal components analysis with varimax rotation of the self-report measures in Table S2 according to CGI-S Social Anxiety rating. Notably, unlike the patterns observed based on principal diagnoses (Table 2) posthoc univariate ANOVA using the CGI severity levels as factors, this time testing the three components of negative affectivity, anxious arousal and social fearfulness, revealed reliable transdiagnostic linear trends across negative affectivity and social fearfulness from the least to most impaired individuals. Not impaired (N =31), minimally impaired (N=9), moderately impaired (N=25), markedly impaired (N=27), and severely impaired (N=13).



Supplemental Figure S3. The percentage of each principal disorder represented at each Clinical Global Impression-Severity (CGS-S) level. Not impaired (N=31), minimally impaired (N=9), moderately impaired (N=25), markedly impaired (N=27), and severely impaired (N=13).

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