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Associations Between Pupillary Response Patterns to Emotional Faces and Self-Reported Social Anxiety

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ASSOCIATIONS BETWEEN PUPILLARY RESPONSE PATTERNS TO EMOTIONAL FACES AND SELF-REPORTED SOCIAL ANXIETY

by

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Under the Direction of Erin B. Tone, PhD

ABSTRACT

The present study examined associations between self-reported social anxiety (SA) and patterns of pupillary response to emotional faces that provided feedback to college student participants (n = 59) about their performance on a reaction time task. I hypothesized that self-reported SA would predict pupil dilation profile (peak, duration, and latency) in response to feedback stimuli of varying intensities (i.e., low vs. high intensity happy and angry). Results showed no evidence of significant associations between peak and sustained pupil diameter measures and SA; however, at 0.5 seconds post-stimulus onset, SA and pupil diameter were negatively associated, such that smaller pupil diameter was associated with higher levels of SA. This pattern could be consistent with a blunted autonomic response to affective cues; examination of concurrent eye-tracking data would provide a test of this possibility. The present study lays crucial groundwork for future assessments utilizing pupil diameter as a parsimonious tool.

INDEX WORDS: Pupil dilation, Social anxiety, Face feedback, Face stimulus intensity

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DEDICATION

This proposal document is dedicated to my family and friends who have been tremendous sources of support throughout my academic and career development. I would not be here without their continued guidance, help, and encouragement.

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TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

1 INTRODUCTION

Pupil dilation, which is a reliable, inexpensive, and parsimonious measure of emotional and cognitive load (Bradley, Miccoli, Escrig, & Lang, 2008), has begun to receive attention as a non-invasive and temporally-sensitive way to examine physiological, particularly brain, reactivity to varied cues in both healthy (e.g., Bijleveld, Custers, & Aarts, 2009) and clinically diagnosed individuals (e.g., Silk et al., 2007). For example, research has yielded consistent evidence that people with depression show atypical patterns of pupillary response to salient affective cues (Siegle et al., 2003a; Siegle et al., 2003b; Siegle, Steinhauer, & Thase, 2004). Moreover, people with schizophrenia show diminished pupillary responses during high-demand cognitive tasks, which might reflect a limitation in attention allocation resources (Granholm et al., 2000, 1997; Steinhauer & Hakerem, 1992; Steinhauer & Zubin, 1982).

There are both theoretical and empirical reasons to believe that similarly clear patterns of pupillary reactivity should be evident in association with anxiety. Theories of anxiety and its maintenance propose that anxious individuals are prone to biased cognition that is characterized by negative interpretation of neutral cues, attention bias to threat, and catastrophizing (Eysenck, 2014; Barlow, 2002). Such negative biases may reflect, at least in part, a heightened sensitivity to potential threat in the environment among people experiencing anxiety, which leaves them with a lower threshold than less anxious peers for perceiving and responding to stimuli as signals of danger (Koster, Crombez, Verschuere, & De Houwer, 2006).

Heightened physiological reactivity in response to salient threat cues may, at least in part, underlie these maladaptive patterns of thought (e.g., Barlow, 2002; Reiss, 1991). In particular, the tendency among anxious people toward negative interpretation of neutral or ambiguous stimuli (Yoon & Zinbarg, 2008) suggests that their perceptual thresholds for identifying stimuli

as threatening might be lower than are those of less-anxious peers. It thus seems plausible that thresholds for pupil dilation—an index of physiological reactivity to threat—should also be decreased. Such lowered thresholds could manifest in any of several ways. First, dilation may be exaggerated or amplified in anxious people when they view images that signal danger. Second, dilation may begin more quickly, given that anxious people show vigilance for danger cues (Mathews, Mackintosh, & Fulcher, 1997). Third, dilation might last longer or be sustained for a longer period of time, given that anxious people tend to dwell on negative thoughts (Stopa & Clark, 2000). Additionally, amplified dilation, dilation latency, and sustained dilation may emerge at a lower threshold; in other words, even mildly threatening images that less anxious people might see as neutral or benign may hold salience for those with high anxiety. Findings from empirical studies regarding pupil dilation to threat cues and anxiety, however, do not consistently support these predictions (e.g., White & Depue, 1999; Hepsomali, Hadwin, Liversedge, & Garner, 2017; Wilson, Smith, Chattington, Ford & Marple-Horvat, 2006; Peavler, 1974).

In the present study, I examined associations between anxiety and pupillary dilation to threat cues, using an archival dataset (n = 59 college students) and a design aimed at minimizing the impact of methodological characteristics that may have contributed to inconsistencies in the extant literature. First, I examined associations between self-reported social anxiety (SA) (rather than general anxiety) and patterns of pupillary response to emotional faces that provided feedback to participants about their performance on a reaction time task, and thus were presumably highly relevant to participants. Second, I capitalized on the use in this task of parametrically morphed emotional faces (50% happy to 50% angry) as feedback cues. By examining participants' pupillary responses to angry faces that varied in intensity, I was able to

evaluate whether SA was associated with distinctive pupillary responses to mild/moderate, as opposed to extreme, facial threat. Findings have potential to inform our understanding of the physiological mechanisms underlying socially anxious cognition and behavior.

In the following sections, I set the stage for my hypotheses and the present study. I first provide background information regarding pupil dilation and how it is conceptualized and measured. I describe the neuroanatomical pupillary pathway, along with functional magnetic resonance imaging (fMRI) data that corroborate this pathway. I then shift focus to findings regarding pupil dilation during presentation of salient cues in studies of healthy and clinically diagnosed individuals, with particular attention to the extant literature regarding pupil dilation and anxiety. Next, I build a case for recruiting a sample characterized with regard to social anxiety (SA), rather than general anxiety or other specific anxiety subtypes. I then describe the present study and hypotheses, clarifying how the use of face stimuli embedded as feedback cues regarding task performance allows for extension of the extant literature. Finally, I present the results of the study, followed by a detailed discussion of the results and their implications, as well as the strengths and limitations of the current study.

1.1 Pupillary Dilation and the Nervous System

The pupil dilates, or expands in size, in response to heightened demands for attention, memory, or general cognitive processing (for reviews, see; Beatty, 1982; Goldinger & Papesh, 2012; Steinhauer & Hakerem, 1992). Further, if cognitive demands or arousal persist, pupil dilation is sustained (Beatty, 1982; Granholm, Asarnow, Sarkin, & Dykes, 1996; Kahneman & Beatty, 1966). Emotional stimuli, which tend to capture attention and to be prioritized for processing, are particularly likely to elicit pupillary responses (Partala & Surakka, 2003; Bradley, Miccoli, Escrig, & Lang, 2013; Proulx, Sleegers, & Tritt, 2017).

Researchers commonly assess pupil dilation according to three parameters. The first of these, peak pupil dilation (the maximum magnitude of pupillary size during presentation of a stimulus), is associated with the level of processing demand (Kahneman, 1973; for a review, see; Beatty, 1982). The second, pupil dilation latency (the amount of time between stimulus onset and dilation) is associated with arousal, such that shorter latency (earlier dilation) suggests heightened arousal in response to a stimulus (Gilzenrat, Cohen, Rajkowski, & Aston-Jones, 2003). Finally, sustained pupil dilation (length of time during which dilation remains at its peak) is associated with persisting processing demands (Granholm, Asarnow, Sarkin, & Dykes, 1996; Kahneman & Beatty, 1966). In other words, dilation tends to last longer when information-processing demands remain.

Increases in processing demands are clearly linked to changes in pupillary response. Emotional and/or salient cues require more effortful processing, which suggest that such cues might elicit heightened pupillary responses. Indeed, Steinhauer and colleagues (1983) examined healthy adults' pupillary responses to a series of pictures that varied in emotional content and found that those stimuli characterized as most aversive or pleasant evoked the largest dilations, while those characterized as mildly pleasant or unpleasant evoked smaller dilations, and neutral pictures evoked the least dilation. Similarly, Aboyoun and Dabbs (1998) presented adults with pictures of clothed and unclothed individuals and found increased pupil dilation during viewing of nude compared to clothed images. These authors interpreted their findings as consistent with the idea that pupil dilation generally reflects the salience or novelty of viewed stimuli.

Given that salient stimuli elicit heightened processing demands among healthy individuals, it seems reasonable to anticipate that particularly exaggerated pupillary response might be elicited from individuals, such as those with high anxiety, who are biased to attend

preferentially to emotional and/or salient cues. Moreover, people who experience anxiety may respond to a wide range of stimuli as threatening; thus, stimuli that less anxious people tend to overlook or ignore may exert emotional or cognitive processing demands on those who are more anxious. In order to conceptualize ways in which the pupil dilation might reflect emotional or cognitive load, I describe the pupillary reflex pathway in detail.

The pupil is located in the center of the iris of the eye. The iris surrounds the pupil and mostly comprises smooth muscle; it controls the size of the pupil in order to regulate how much light enters the eye. The iris accomplishes this task using two groups of smooth muscles: the sphincter muscle and the dilator muscle. When the sphincter muscle is stimulated, the iris constricts or decreases the size of the pupil. Conversely, when the dilator muscle is stimulated, the iris expands or increases the size of the pupil (Hughes, 1991).

The muscles of the iris act in response to signals from the parasympathetic nervous system (PNS; sometimes called the "rest and digest system" due to its role in conserving energy by, for instance, lowering heart rate and increasing gastrointestinal activity). Simultaneously, they receive parallel input from the sympathetic nervous system (SNS; the "fight or flight system" involved in preparation for a threat response via such changes as increasing heart rate and constricting blood vessels). Activity in both pathways that terminates in pupillary changes begins with perception of a visual stimulus (Kaufman, Levin, Adler, & Alm, 2011).

Depending on the characteristics of the stimulus that triggers pupillary activity, the pupil dilates or constricts. In response to stimuli that demand attention or elicit arousal, signals transmitted via the PNS pathway inhibit the sphincter muscle of the iris, whose role is to constrict the pupil; this input makes dilation possible. At the same time, signals traveling through the SNS pathway stimulate the dilator muscle of the iris, whose role is to expand the

pupil (See Figure 1.1). In contrast, in response to stimuli such as light, signals traveling via the PNS pathway stimulate the sphincter muscle of the iris (leading to increased constriction), while signals traveling through the SNS pathway simultaneously inhibit the dilator muscle of the iris (allowing for increased constriction). The extent to which cognitive or affective processing is driven by either the SNS or the PNS pathway is unclear (Steinhauer, Siegle, Condray, & Pless, 2004), and it is possible that both pathways are involved in responses during all cognitive or affective tasks.

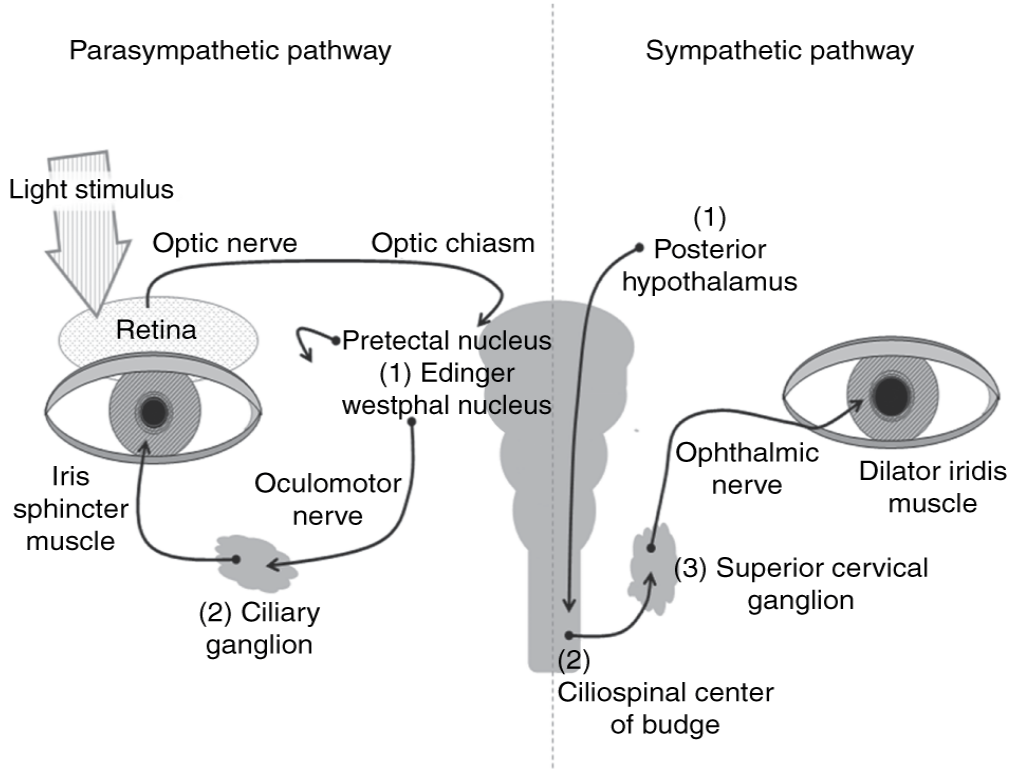

Figure 1.1 Neural Pathways of Pupil Dilation
Note. Reprinted from "Pupillometry in congenital central hypoventilation syndrome (CCHS): quantitative evidence of autonomic nervous system dysregulation," by P.P. Patwari et al., 2012, Pediatric Research, 71 *(3). Copyright 2012 by Springer Nature. Reprinted with permission.*

Various brain regions send signals through the pupillary response pathway, helping to determine whether the pupil dilates or constricts. Signals generated in the PNS pathway following perception travel through the optic nerve to the pretectal nucleus of the midbrain,

which serves as a relay station. This nucleus also mediates the pupillary light reflex, a basic response that controls the diameter of the pupil, allowing for adaptation to various levels of light and darkness (Purves et al., 2008). The signal continues to the Edinger-Westphal nucleus of the oculomotor complex, the point of origin for nerve fibers that control the constriction and dilation of the iris sphincter muscles.

Concurrently triggered signals within the SNS pathway travel through the optic tract fibers and stimulate neurons in the hypothalamus, which coordinates autonomic nervous system and pituitary activity (e.g., controlling body temperature, thirst, and hunger), to indicate whether the iris dilator muscles should contract or relax. SNS signals travel through the spinal cord and two subsequent relay points (the sympathetic preganglionic neurons and the superior cervical ganglion), finally terminating at the iris dilator muscles. Depending on the confluence of signals from the two nervous system pathways, the pupils will either dilate or constrict.

Activity in both the PNS and SNS pathways is modulated by signals from a number of distinct cortical regions that process stimulus characteristics. The PNS pathway receives input at the oculomotor nucleus primarily from the amygdala, a region commonly implicated in the experiencing of emotions, faces, and novelty cues (for a review, see; Zald, 2003; See Figure 1.2). The amygdala's signals are modulated by input to that region from the anterior cingulate cortex (ACC; implicated in emotional self-control, problem-solving, error recognition, adaptive responses; for a review, see; Allman, Hakeem, Erwin, Michinsky, & Hof, 2006) and the dorsolateral prefrontal cortex (dlPFC; implicated in working memory; Mars & Grol, 2007). As expected, given this pattern of connectivity, studies show evidence that pupil dilation is associated with patterns of activity in the amygdala (Koikegami & Yoshida, 1953), ACC

(Critchley, Tang, Glaser, Butterworth, & Dylan, 2005), and dlPFC (Siegle, Steinhauer, Stenger, Konecky, & Carter, 2003b).

Additional input to the PNS pathway comes from the precuneus, a region whose functions are not fully understood, but that appear to encompass elements of visuo-spatial imagery, episodic memory retrieval, self-processing, and consciousness (for a review, see; Cavanna & Trimble, 2006). The precuneus, which is located between the somatosensory cortex and the cuneus (which houses the visual cortex), sends signals to the pretectal area of the pathway. Activation of the precuneus has been associated with latency of peak pupillary dilation during an auditory oddball task (Book, Stevens, Pearlson, & Kiehl, 2008).

Like the PNS pathway, the SNS pathway receives direct input from varied brain regions. Much of the input to this pathway likely occurs at the hypothalamus (See Figure 1.2), which receives signals from the amygdala, and thus, indirectly, from the ACC and dlPFC as well. In an additional parallel to the PNS pathway, the hypothalamus receives signals directly from the ACC and the precuneus.

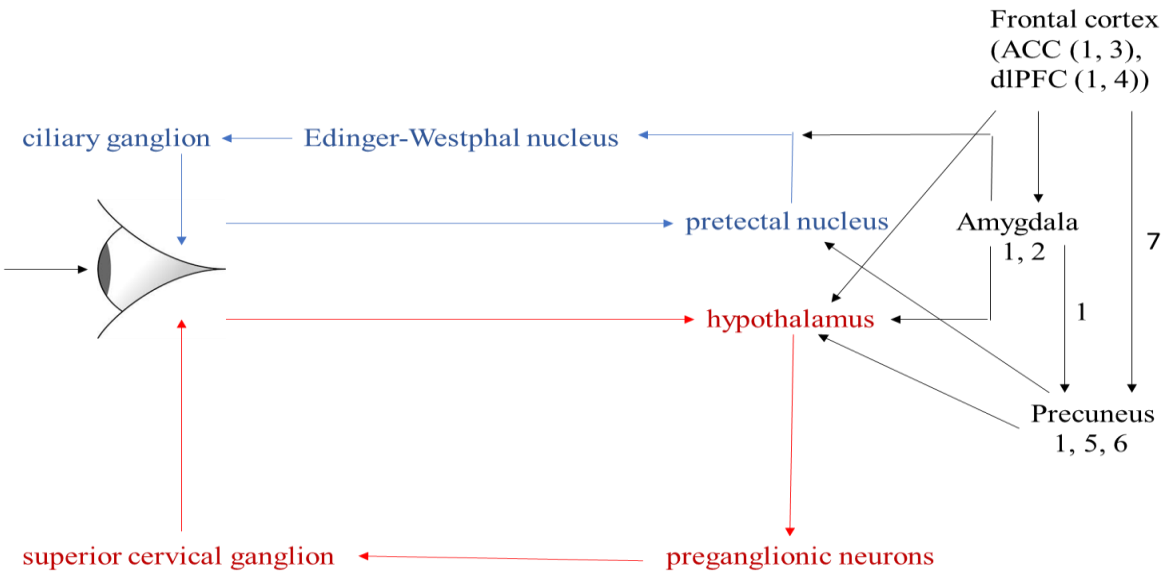

Figure 1.2 Neural Pathways of Pupil Dilation and the Integration of Additional Brain Regions Involved

Note. Red denotes the sympathetic pathway. Blue denotes the parasympathetic pathway. 1. Bruhl et al., 2014. 2. Koikegami & Yoshida, 1953. 3. Critchley, Tang, Glaser, Butterworth, & Dylan, 2005. 4. Siegle, Steinhauer, Stenger, Konecky, & Carter, 2003b. 5. Muller-Pinzler, Gazzola, Keysers, Sommer, Jansen, Frassle, Eihauser, Paulus, Krach, 2015. 6. Book, Stevens, Pearlson, & Kiehl, 2008. 7. Pannekoek, Veer, van Tol, van der Erff, Demenescu, Aleman, Veltman, Zitman, Rombouts, van der Wee, 2013; Bruhl et al., 2014. ACC-anterior cingulate cortex; dlPFC-dorsolateral prefrontal cortex.

Additional brain regions appear to participate in regulating both PNS and SNS pupillary response pathways. One such region is the locus coeruleus (LC), which sends direct input to the SNS pupillary pathway via the preganglionic neurons; simultaneously, the LC regulates PNS pathway activity by sending inhibitory signals to the Edinger-Westphal nucleus (Szabadi, 2012). The LC has been implicated in arousal (Berridge & Waterhouse, 2003), varied aspects of cognitive processing (Carter et al., 2010; Hickey et al., 2014; Snyder et al., 2012; Valentino & Van Bockstaele, 2008; Vazey & Aston-Jones, 2014), and pupillary reactivity (Joshi, Kalwani, & Gold, 2016; Reimer et al., 2016, Aston-Jones & Cohen, 2005; Nassar et al., 2012) although evidence of the latter association is largely indirect (Joshi, Li, Kalwani, & Gold, 2016). Notably,

research also suggests that the LC is a critical player in the transmission of information about stress and the production of anxiety-related behavior under stressful circumstances (McCall et al., 2015). It thus appears possible that the LC plays a role in mediating humans' anxiety-related pupillary responses to threat cues; however, studies have yet to test this hypothesis.

1.2 Pupillary Response Patterns and Psychopathology

The literature to date provides evidence of distinct patterns of association between pupillary activity and some types of psychological disorders and symptom types. In particular, substantive bodies of research link distinctive patterns of pupillary activity to both depression and schizophrenia. Compared to healthy controls, for example, individuals diagnosed with unipolar major depression show more exaggerated peak dilation to negative and personally-relevant negative words (Siegle et al., 2003a), and longer sustained dilation when viewing negative and personally-relevant stimuli (Siegle et al., 2003b). Further, relative to controls, depressed individuals display a more substantial decrease in pupil dilation in the seconds following stimulus presentation during the Stroop task (Siegle, Steinhauer, & Thase, 2004). Some evidence suggests that atypical pupillary dilation patterns could serve as a marker of depression risk. In one recent 24-month longitudinal study of children with depressed mothers, for instance, children who demonstrated greater peak pupil dilation to sad faces at baseline maintained their depressive symptoms over the two-year period. Moreover, they showed a shorter time to depression onset, compared to those children who demonstrated lower pupil dilation to sad faces and who exhibited a decline in depressive symptoms over the same two-year period (Burkhouse, Siegle, Woody, Kudinova, & Gibb, 2015).

Similarly, consistent evidence has emerged regarding associations between schizophrenia and atypical pupillary dilation. In particular, affected individuals show smaller pupillary

responses than do healthy individuals during cognitive tasks that place high processing demands (Granholm et al., 1996, 1997; Steinhauer & Hakerem, 1992; Steinhauer & Zubin, 1982). Researchers have suggested that this pattern of attenuated task-related pupillary response among individuals with schizophrenia may reflect the diminished attentional resources that they can bring to bear when tasks carry higher cognitive loads (Granholm et al., 1996, 1997; Walker & Harvey, 1986).

Findings in more recent years lend support to this suggestion. For example, Granholm and colleagues (2000) found that patients with schizophrenia showed poorer performance and lower average total pupil dilation (indicating reduced resource allocation) than non-patients, but only during a working memory task (span of apprehension task) that required high cognitive effort. In another study from the same group, smaller average pupil dilation was associated with both reduced response complexity on a visual processing task (Rorschach blots) and more severe thought disorder, defined as cognitive fragmentation and thought disturbances (Minassian, Granholm, Verney, & Perry, 2004). Thus, the literature suggests that in people with schizophrenia, more disrupted cognitive performance (as indicated by attention allocation difficulties, etc.) during tasks that demand high cognitive effort and processing is associated with attenuated average pupil dilation. Some researchers have asserted that this pattern may stem from reduced overall resources (Granholm, Fish, & Verney, 2009). They point also, however, to the alternate possibility that it could reflect misallocation of resources, or wasteful use of resources on low cognitive demands, which leaves fewer resources for tasks that demand more cognitive effort (Granholm & Verney, 2004; Granholm, Morris, Asarnow, Chock, & Jeste, 2000). The accuracy of these explanations remains uncertain; however, it is clear that measures

of pupil dilation provide useful insight into attention allocation and cognitive performance among individuals with schizophrenia.

In contrast to the clear and consistent patterns of pupillary activity observed in depression (exaggerated pupillary responses to negative cues) and schizophrenia (dampened pupillary responses during demanding cognitive tasks), associations between pupil dilation and anxiety have varied across studies (See Table 1.1). This variability could indicate that the ways in which anxiety relates to pupillary dilation are especially complex and difficult to capture. It may also, at least in part, reflect differences among studies to date along several parameters.

First, researchers studying anxiety and pupillary responses have gathered pupillary data while participants completed a variety of tasks (e.g., digit span, driving simulation, face/word viewing) that vary in their cognitive and emotional demands. Second, stimulus content (e.g., words, faces displaying different emotions) during these tasks has also been inconsistent. Third, there is surprising variability across studies in the dilation parameters reported, with different studies providing data about peak dilation, dilation latency, or sustained dilation, but few addressing all three. Fourth, whereas some studies have examined pupillary activity during experimental conditions and paradigms that elicit anxiety in student or community samples recruited without regard to their levels of anxiety, others have compared patterns of dilation between groups of individuals selected based on how anxious they tend to be (high vs. low).

Given this substantial variability in study parameters, it is difficult to extract coherent themes from the published research on pupillary dilation and anxiety. Outcome measures (peak dilation, dilation latency, sustained dilation), while not reported uniformly across studies, offer one informative way to organize study results. Therefore, in the following paragraphs, I present

a brief overview of the literature on anxiety and pupil dilation literature, with findings organized according to pupil dilation parameters.

Most previous research assessing the relationship between pupillary activity and anxiety has focused on average or peak pupil diameter, or on the magnitude of change in size from a predetermined baseline. Early research suggested that demanding cognitive tasks elicit amplified dilation for anxious individuals, in marked contrast to the attenuated responses observed in adults with schizophrenia. In one study, for example, adults with high fear of negative evaluation showed elevated peak dilation during a challenging mental arithmetic task (Simpson & Molloy, 1971). More recently, high compared to low trait anxious adults showed larger pupil diameter in response to a simulated driving task in low (non-evaluative driving task) and high (subjects were told that their performance was to be compared with that of others) threat conditions (Wilson et al., 2006).

Findings from some studies also link anxiety, much like depression, to amplified peak dilation in response to salient, negatively-valenced cues, particularly faces that signal the presence of threat in the environment. Anxious youths diagnosed with Generalized Anxiety Disorder, Social Anxiety Disorder, or Social Phobia, for example, showed increased peak pupil dilation relative to low-anxious peers when a fixation dot replaced fearful faces (considered indirect indices of threat presence) in a dot-probe task measuring attention bias (Price et al., 2013). Additionally, one study found that adults' trait anxiety measured by the State-Trait Anxiety Inventory (STAI) was positively associated with pupil size following the presentation of angry faces (Kret, Stekelenburg, Roelofs, & de Gelder, 2013). A third study showed that youths with higher levels of anxiety, measured by the Screen for Child Anxiety Related Disorders (SCARED), showed larger pupil dilation (calculated as the difference between peak and baseline

dilation) following the presentation of an emotional word than did those low in anxiety. However, the same study did not find similar differences between adults with low and high levels of anxiety (Shechner et al., 2015).

Contributing to the inconsistency, one study that compared healthy individuals and youth with an anxiety disorder during a virtual peer interaction task found no between-group differences in pupil dilation during personally-relevant rejection trials, contrary to hypotheses (Rosen, 2012). Similarly, in a sample of college students grouped according to self-reported anxiety, Hepsomali and colleagues (2017) failed to detect predicted differences between high and low anxious individuals in their peak responses to angry face cues. Instead, they observed an overall increase in peak dilation and elevated sustained dilation in response to emotional cues in general among high anxious participants. Furthermore, at least one study showed that individuals with high trait anxiety showed a pattern of attenuated pupillary reactivity relative to low-anxious peers when they were faced with volatile changes in the probability of receiving a shock after making a choice between two stimuli, one of which was associated with punishment on each trial (Browning et al., 2015). In other words, those with high trait anxiety showed smaller pupillary dilation in response to environmental volatility than those with low trait anxiety. These mixed findings in samples of youths and adults raise questions about whether or not pupil dilation patterns differ between anxious and healthy individuals.

The literature regarding sustained dilation and dilation latency is clearer. Few studies have presented associations between anxiety and indices of sustained dilation or dilation latency, but the sparse extant findings suggest that dilation could be slower and more protracted in anxious individuals than in controls during viewing of threat-related cues. For example, in an early study, Peavler (1974) found that when healthy participants were required to recall long

strings of digits, a requirement typically thought to evoke an anxious response, pupil dilation was sustained rather than increased. More recently, Price and colleagues (2013) observed similarly persistent responses in anxious youths, who showed consistently sustained pupil dilation following the presentation of fearful/neutral face pairs during a dot-probe task, regardless of which face the probe replaced (Price et al., 2013). This pattern contrasted with that of non-anxious control participants, who showed sustained pupil dilation only during trials when the probe replaced neutral rather than fearful faces; the authors interpreted this contrast as suggestive of an "inflexible" pattern of pupillary responding in anxious participants. Hepsomali et al. (2017) obtained evidence of similarly sustained dilation in adults with high self-reported anxiety while they viewed emotional faces; moreover, peak pupillary responses to emotional faces were also slower for high compared to low anxious individuals in this study (Hepsomali et al., 2017).

Taken together, across this small literature, the most frequently observed finding has been a pattern of amplified peak dilation in response to visual cues of threat, such as angry faces or words, in association with anxiety symptoms or diagnoses (Price et al., 2013; Shechner et al., 2015). In contrast, several studies have found no evidence of differential responses between anxious and healthy youth (Rosen, 2012) and adults (Shechner et al., 2015; Hepsomali et al., 2017), and at least one has found an attenuated response in anxious compared to healthy adults (Browning et al., 2015). There is considerable evidence that anxiety relates to excessively sustained dilation to salient cues. Given these inconsistent patterns, the literature raises questions about the degree to which pupil dilation patterns provide insight into anxiety-related cognitive and perceptual processes.

Table 1.1 Patterns of Pupil Dilation Associated with Anxiety and Related Processes

Authors (year)	Title	Task/Stimuli	Parameter	Findings
Peavler (1974)	Pupil Size, Information Overload, and Performance Differences	A digit span task requiring immediate recall	Average pupil diameter	Dilation associated with longer digit strings thought to elicit overload or anxiety (13 vs 9) appeared to stay the same rather than increase
Wilson, Smith, Chattington, Ford, Marple-Horvat (2006)	The role of effort in moderating the anxiety-performance relationship: Testing the prediction of processing efficiency theory in simulated rally driving	Low- and high-threat driving simulation task	Average pupil diameter	Pupil diameter was greater for high compared to low trait anxious individuals and greater under the high compared to the low pressure condition.
Kimble, Fleming, Bandy, Kim, Zambetti (2010)	Eye tracking and visual attention to threatening stimuli in veterans of the Iraq war	Split screen task-negative valence pictures (war related image and motor vehicle accident (MVA) image), and neutral pictures	Average pupil diameter	Iraq war veterans higher in PTSD measured by the PTSD symptoms scale showed larger pupil dilation to both negatively valenced pictures (war-related and MVA)
Price, Siegle, Silk, Ladouceur, McFarland, Dahl, Ryan (2013)	Sustained Neural Alterations in Anxious Youth Performing an Attentional Bias Task	Dot-probe task/neutral and fearful faces	Average pupil diameter, Sustained dilation	Sustained pupil dilation in anxious youth was observed when the dot replaced fearful faces. This was accompanied by an “inflexible” pattern of responding in comparison to controls, whereby non-anxious control individuals showed greater sustained pupil dilation during incongruent trials whereas pupil dilation waveforms in the anxious group remained fairly stable regardless of dot-location.

Kret, Stekelenburg, Roelofs, de Gelder (2013)	Perception of Face and Body Expressions Using Electromyography, Pupillometry and Gaze Measures	Emotional face and body viewing/fearful, happy, and angry facial expressions and corresponding bodily expressions	Average pupil diameter	Anxiety measured by the STAI was positively associated with pupil size in response to angry face cues.
Burkhouse, Siegle, Gibb (2014)	Pupillary reactivity to emotional stimuli in children of depressed and anxious mothers	Emotional face viewing/sad, happy, angry, neutral faces	Average pupil diameter	Children of anxious mothers showed increased pupil dilation to angry, but not happy or sad faces. At high emotional intensity (vs. low and medium), there was a significant main effect of anxiety for angry faces.
Shechner, Jarcho, Wong, Leibenluft, Pine, Nelson (2015)	Threats, rewards, and attention deployment in anxious youth and adults: An eye tracking study	Visual Scene Task- reward and threat scenes Negative Words Task- negative social (e.g. lonely, bully), negative non-social (e.g. poison, hurt), and neutral words	Average diameter change	No main or interaction effects were detected for pupil dilation during a Negative Word Task; however, for youths only, maximal change in pupil dilation was positively associated with SCARED score. In other words, greater anxiety symptoms among youth were associated with greater physiological responsiveness to threat.
Browning, Behrens, Jocham, O'Reilly, Bishop (2015)	Anxious individuals have difficulty learning the causal statistics of aversive environments	Two-armed bandit learning task. Subjects chose one of two gabor patches, either of which resulted in an electrical shock	Average pupil diameter	Post-outcome dilation was greater for more compared to less volatile and surprising environments. However, individuals with high trait anxiety showed a general deficit in learning rate and a smaller effect of environment volatility on post-outcome dilation.
Hepsomali, Hadwin, Liversedge, Garner (2017)	Pupillometric and saccadic measures of affective and executive processing in anxiety	Emotional face viewing/angry, fearful, happy, neutral faces	Peak dilation Dilation latency	Peak pupillary responses to faces were larger (but slower/higher latency) for high-anxious individuals compared to low-anxious individuals. However, all individuals displayed

				larger peak responses to angry compared to happy faces, regardless of level of anxiety.

Although there are commonalities among studies of pupillary dilation and anxiety in terms of methodological characteristics (e.g., many use emotional faces as stimuli), their diversity with regard to methodology is striking. It is possible that the diversity of approaches to studying anxiety-related pupillary-dilation obscures patterns of association (or lack thereof) between level of anxiety and pupillary response in any of several ways. First, some studies that used emotional faces (angry, happy, fearful) as stimuli included only extreme exemplars of each expression. It is possible that these exaggerated depictions of emotion elicited similarly heightened responses from low and high anxious individuals; subtle expressions, particularly of negative emotions such as anger, might be arousing for those with high anxiety, but not those who are less anxious. Therefore, an assessment of the threshold of stimulus intensity at which a pupillary response is elicited might offer more meaningful information regarding group differences. Second, all of the above studies assessed differences in pupil dilation between individuals who report low and high general anxiety. While general anxiety may indeed be linked to pupillary dilation anomalies, differences in pupillary reactivity to emotional cues, particularly angry faces, may be more readily evident between people who report high and low SA, as socially anxious individuals display heightened sensitivity to such cues (Mogg, Philippot, & Bradley, 2004). Third, socially anxious individuals tend to be particularly sensitive to personally-relevant feedback (Clark & Wells, 1995; Rapee & Heimberg, 1997). Embedding putative threat cues, such as angry faces, in the context of feedback that is personally salient may increase the likelihood of detecting pupillary differences between low and high socially anxious individuals in response to such cues.

To provide a step toward resolving inconsistencies in the anxiety and pupillary dilation literature, I specified the design of the proposed study in ways intended to maximize the

likelihood that I could detect pupillary dilation patterns that may be specific to anxiety. First, I focused narrowly on one type of anxious cognition/behavior—SA, which is typically characterized by fear of negative evaluation and avoidance of social situations in which such evaluation might occur (American Psychiatric Association, 2013). This construct lends itself readily to the examination of pupillary dilation in response to emotional faces, because such cues should be highly relevant to individuals with elevated symptoms.

SA is widely prevalent, at both clinical and subclinical levels. Its most extreme presentation, termed social anxiety disorder (SAD; DSM-5; American Psychiatric Association, 2013) or, historically, social phobia (DSM-IV; American Psychiatric Association, 2000), has a lifetime prevalence of 2-13%, making it one of the most common anxiety disorders (Kessler et al., 2005). As much as an additional 20% of the general population, however, endorses one or more SA symptoms, particularly fear and avoidance of public speaking (55%), addressing familiar groups (24.9%), or interacting with people in authority (23.3%). Other social fears that people commonly endorse include attending social gatherings (14.5%), meeting new people or speaking to strangers (13.7%), and eating (7.1%) or writing (5.1%) in front of people (Stein, Walker, Forde, 1994).

Well-established cognitive models of SA (Clark & Wells, 1995; Hofmann, 2007; Rapee & Heimberg, 1997; Heimberg et al., 2010) propose that socially anxious people should interpret external social events as negative, catastrophize about the consequences of negative social cues, and preferentially recall negative information regarding how they are perceived (for a review, see; Clark & McManus, 2002). In one of the earliest models, Clark and Wells (1995) hypothesized that socially anxious individuals demonstrate hypervigilance to external social cues that they likely interpret negatively. A parallel, and complementary, model (Rapee & Heimberg,

1997) proposed that the socially anxious person demonstrates heightened self-focus based on long-term recollection of prior experience, internal cues (e.g., physiological reactivity), and external cues (i.e., audience feedback). In addition to this self-focus, the individual attends specifically to potential external threats (e.g., frowns). More recent efforts to integrate and extend these models suggest that lack of self-confidence and increased self-focus trigger a number of additional aberrant cognitive processes, including overestimating the potential social costs and exaggerating the likelihood of a negative evaluation (Hofmann, 2007), as well as catastrophizing about the social outcomes associated with exposing their perceived self-deficiency (Moscovitch, 2009). Empirical studies have lent support to these theories, by showing that socially anxious individuals have a tendency to attend preferentially to negative stimuli, such as angry facial expressions (Bar-Haim, Lamy, Pergamin, Bakermans-Kranenburg, & van IJzendoorn, 2007), to interpret ambiguous social events as threatening (Yoon & Zinbarg, 2008), and to catastrophize about mildly negative social events (Stopa & Clark, 2000). SA thus appears to provide a useful starting place for evaluating associations between symptoms and patterns of pupillary responses to a range of threat cues.

A second way in which I attempted to maximize the likelihood of detecting patterns of pupillary dilation associated with anxiety was by assessing reactivity to emotional faces that range in intensity from neutral to intensely expressive. In light of evidence that socially anxious individuals preferentially detect and attend to threatening cues (Bar-Haim, Lamy, Pergamin, Bakermans-Kranenburg, & van IJzendoorn, 2007) and that they tend to negatively interpret neutral cues (for a review, see; Clark & McManus, 2002), I anticipated that participants who endorsed high levels of SA would show distinctive pupillary reactions, not only to prototypical and extreme exemplars of anger, but also to subtler angry expressions that individuals lower in

SA might perceive as benign. Finally, unlike most of the earlier studies of pupillary dilation and anxiety, I planned to examine the full time course of the pupillary response, including peak dilation, dilation latency, and dilation duration.

1.3 Aims of the Present Study

I designed the present study to help clarify whether anxiety—SA in particular—is associated with an exaggerated pupillary response to threat cues. I examined, using archival data from a sample of 59 college students, associations between self-reported SA and patterns of pupillary response to photographed faces that were morphed to vary in valence along spectra from happy to neutral and neutral to angry. Participants viewed the faces in the context of a challenging reaction time task; faces provided feedback to participants about the accuracy and speed of their responses on the preceding five reaction time trials.

I hypothesized that individuals higher in SA would display a distinctive pattern of pupillary response, such that peak dilation and dilation duration in response to subtly threatening evaluative faces (10%-50% angry) would be greater, while dilation latency would be shorter for participants higher in SA than for those lower in SA. Given inconsistencies in the literature regarding pupillary patterns in response to extreme facial expressions, I did not speculate on the magnitude or direction of a difference in pupillary patterns in response to extreme face cues. In addition to having a larger sample size than most previous studies, the present study was built around a task that provides self-relevant and evaluative feedback, cues that individuals experiencing SA are particularly sensitive to (Rapee & Heimberg, 1997; Hofmann, 2007). Pupillary patterns associated with a range of emotional stimuli are likely to provide a more a holistic view of the subtleties of SA and, in turn, to have implications for intervention. I tested the following hypotheses:

1.3.1 Specific Aim 1: Examine the association between peak dilation and stimulus intensity for individuals at varying levels of SA (i.e. -1 (low), -0.5 (mild), 0.5 (moderate), and 1 (high) standard deviations below or above the mean).

Hypothesis 1: Given that SA is associated with strong emotional reactions and hyper-arousal in response to neutral stimuli, as well as a bias to evaluate those stimuli negatively, I expect that peak dilation will be greater for individuals higher in SA than for those lower in SA.

Hypothesis 2: Given that SA is associated with negative interpretation of neutral stimuli, I expect that level of SA (low, mild, moderate, and high) will interact with level of facial expression intensity (50% happy-50% angry) to predict peak dilation, such that the relationship between peak dilation and stimulus intensity will be stronger for those higher in SA (moderate and high) than for those lower in SA (low and mild).

1.3.2 Specific Aim 2: Examine the association between dilation duration and stimulus intensity for individuals at varying levels of SA (i.e., low, mild, moderate, high).

Hypothesis 1: Given that SA is associated with persistent fear of negative evaluation and catastrophizing, I expect that dilation duration will be longer for individuals higher in SA than for those lower in SA.

Hypothesis 2: I expect that level of SA (low, mild, moderate, and high) will interact with level of face intensity (50% happy-50% angry) to predict dilation duration, such that the relationship between dilation duration and stimulus intensity will be

stronger for those higher in SA (moderate and high) than for those lower in SA (low and mild).

1.3.3 Specific Aim 3: Examine the association between dilation latency and stimulus intensity for individuals at varying levels of SA (i.e., low, mild, moderate, high).

Hypothesis 1: Given that SA is associated with preferential attention to negative stimuli, I expect that dilation latency will be shorter for individuals higher in SA compared to those lower in SA.

Hypothesis 2: I expect that level of SA (low, mild, moderate, and high) will interact with level of face intensity (50% happy-50% angry) to predict dilation latency, such that the relationship between dilation latency and stimulus intensity will be stronger for those higher in SA (moderate and high) compared to those lower in SA (low and mild).

Table 1.2 Predicted Patterns of Pupil Dilation for SA

	Peak Dilation	**Dilation Latency**	**Dilation Duration**
Stimulus Intensity (positive to negative)	Stronger positive association for higher SA compared to lower SA	Stronger negative association for higher SA compared to lower SA	Stronger positive association for higher SA compared to lower SA

2 METHODS

2.1 Procedures

2.1.1 Participant Screening and Recruitment

Participants were undergraduate students recruited from introductory psychology courses at an urban university. All participants provided informed consent and received course credit for

their participation in the study. See Table 2.1 for a summary of participant demographic information.

Table 2.1 Participant Characteristics

N (# of participants)	59
Sex (% Male)	14.5%
Race (% White)	27.6%
Race (% Black)	51.1%
Race (% Asian)	14.5%
Ethnicity (% Hispanic or Latino)	6.9%
Age at examination (SD)	20.69 (4.37)
Current year in college (% Freshman)	38.2%
Current year in college (% Sophomore)	34.5%
Current year in college (% Junior)	20.0%
Current year in college (% Senior)	7.3%

2.1.2 Eye Tracking Recording

All recordings were obtained in a single room, lit by standard overhead fluorescent lights. Pupil dilation was recorded using an Applied Science Laboratories (ASL) Model 504 eye tracker, which is equipped with remote pan tilt optics. The tracker sampled eye position with precision better than an 0.5 degree visual angle and less than one degree of spatial error. Eye position was sampled at 120 Hz. A chin rest and autofocusing lens were used to minimize the possibility of artifacts due to head movements. Use of the chin rest also ensured a consistent distance of 19 inches from the eye to the screen across participants.

2.1.3 Pupillary Data Processing

I processed raw eye movement data using the EYENAL Data Analysis Program, a proprietary software program supplied by ASL (Applied Science Laboratories [ASL] Model 504, Boston). The program calculated fixations (gazes) based on an algorithm that accounts for the distance from the eye to the screen, which in this case was kept uniform across participants (19 inches).

Pupillary dilation data were cleaned in MATLAB using a standard script that has been used in multiple published studies (e.g., Siegle, Granholm, Ingram, & Matt, 2001; Siegle, Steinhauer, Carter, Ramel, & Thase, 2003). Blinks were identified as large pupil diameter changes that occurred too rapidly to constitute true dilation or constriction. In accordance with standards in the field, trials comprising more than 50% blinks were removed and linear interpolations were used to replace blinks throughout the dataset. Linear trends in pupil dilation over trials were removed to eliminate slow drift effects (linear trends that are unrelated to trial characteristics) and artifacts (for example, pupil diameters that were out of physiologically plausible range, i.e., smaller than 1mm or larger than 9mm).

I analyzed each subject's pupil dilation waveform for each image in each emotion category (low happy, high happy, low angry, high angry) with the exception of neutral trials, of which there were too few to examine. Consistent with standard data extraction procedures (Siegle et al., 2003), I averaged pupil diameter across the stimulus presentation time window in 0.5-second increments for each stimulus valence group. This approach allowed me to assess changes in pupil diameter across the response time-window in increments that allow for sufficient time to capture physiologically meaningful changes, given the typical response latency of 0.1-0.5 seconds to changes in mental workload (Wang, 2011). These averaged values served as independent variables in statistical analyses.

2.1.4 Assessment of Social Anxiety

SA was assessed using the Self-Report Version of the Liebowitz Social Anxiety Scale (LSAS-SR; Baker, Heinrichs, Kim, & Hofmann, 2002). Participants each completed the 24-item self-report measure of fear and avoidance in social and performance situations, rating each situation on a 4-point Likert-type scale, with 0 indicating no fear or avoidance and 3 indicating

severe fear or avoidance. Total scores can range from 0-144, with scores for each subscale (fear, avoidance) ranging from 0-72. Internal reliability estimates range from .88 to .95 (Oakman, Van Ameringen, Mancini, & Faryolden, 2003).

The psychometric properties of the LSAS-SR were assessed in the present sample. Scores on the Fear Subscale ranged from 2 to 61 and averaged 25.18 (*SD* = 11.56), while scores on the Avoidance Subscale ranged from 2 to 57 and averaged 25.46 (*SD* = 11.89). Total LSAS-SR scores ranged from 8 to 116, with an average of 51.87 (*SD* = 22.78). The LSAS-SR showed high internal consistency reliability in the present sample (α = 0.926 overall, α= 0.891 for the Fear Subscale, and α = 0.866 for the Avoidance Subscale). The subscales of the LSAS-SR were also strongly correlated with each other (r = .715, p < .01).

2.1.5 Face Feedback Task Description

Participants completed the 375-trial computerized Face Feedback Task (FFT), which is a reaction time/accuracy and self-evaluation measure. The task was presented on a desktop PC using Eprime 1.1 (Psychology Software Tools). Each trial consisted of a gray or white asterisk that appeared in randomly assigned locations on the screen. Participants were instructed to hit the space bar as quickly as possible when a white asterisk appeared and to refrain when a gray asterisk appeared.

After every five reaction time trials, participants were shown a screen that asked, “How did you do?”. Participants then rated their performance on the preceding five trials using a mouse-controlled slider bar. The bar’s scale was anchored by the words “poor” and “great” on opposite poles. The slider always began in the center of the bar, and the participants moved it to the point that they thought reflected their performance. They then right-clicked on the mouse to record the response. The click indicated a rating between 0 and 100. Given that there are 375

reaction time trials in the task, each participant completed 75 self-ratings. The first 15 ratings were completed in the absence of objective feedback about the participant's actual performance (see Figure 2.1).

During feedback trials (60 ratings), a black and white emotionally expressive face filled the top half of the screen in a 5.7" x 7.7" window. Faces used for feedback were selected from the NimStim (Tottenham et al., 2009) stimulus set. Four female and four male models were used, and each model's neutral face was morphed with his or her own happy and angry face photographs using Morpheus Photo Morpher software (Morpheus Software). This process yielded a set of faces that varied consistently along a gradient from happy to angry. For each model, three "happy" photographs (50% happy/50% neutral, 40% happy/60% neutral, 30% happy/70% neutral), three "angry" photographs (50% angry/50% neutral, 40% angry/60% neutral, 30% angry/70% neutral), and five "neutral" photographs (20% happy/80% neutral, 10% happy/90% neutral, 100% neutral, 20% angry/80% neutral, 10% angry/90% neutral) were used in the task.

During feedback ratings, the face that appeared provided evaluative information about the speed and accuracy with which the participant had performed on the preceding five trials. Each face remained on the screen until the participant had rated his or her own performance. When participants hit the space bar for a gray asterisk (commission error) or failed to hit the space bar for a white asterisk (omission error) and/or when their mean time for the five trials was at least 50 milliseconds slower than on the previous set of 5 trials, they were shown an angry face, which was randomly selected from the set of "angry" images. When the participant's reaction time was faster in the five trials than it had been in the previous set of five trials by at least 50 milliseconds and the participant made no omission or commission errors, a happy face, randomly selected

from “happy” images, appeared on the screen during rating. When the participant’s mean reaction time in the five trials was within 50 milliseconds of the previous trials’ mean reaction time (in either direction) and the participant made no errors, a “neutral” face appeared.

The task yields data regarding accuracy, response time, and performance self-evaluation. Accuracy was calculated by combining commission and omission errors and subtracting the total number of errors from total trials. Performance self-assessment was calculated from mean self-ratings for no-feedback, negative feedback, and positive feedback conditions. For the purpose of the current study, I assessed pupillary dilation data collected during the three feedback conditions.

2.2 Analyses

2.2.1 Power Analysis

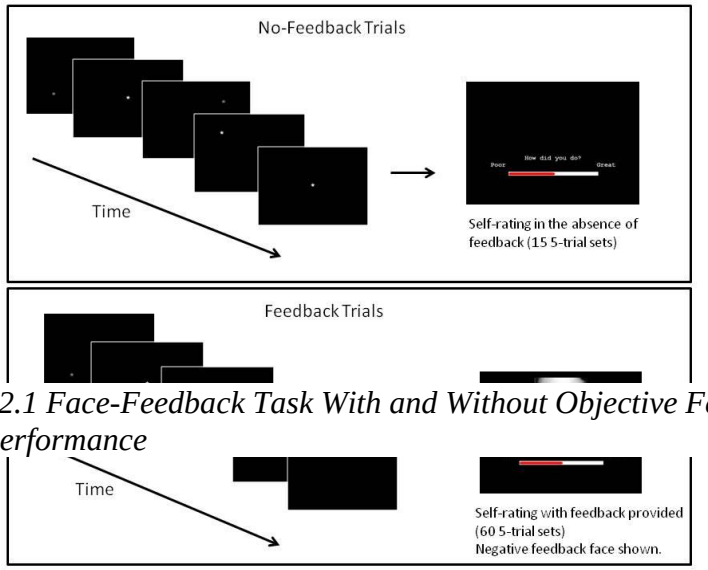

Figure 2.1 Face-Feedback Task With and Without Objective Feedback About Participants' Performance

I conducted a post hoc power analysis using the program *G*Power* (Erdfelder, Faul, & Buchner, 1996) to determine if the current study was adequately powered to detect an interactive effect of SA and image valence on pupil dilation. Given the sample size of 59, I was adequately powered ($1-\beta = .80$) at the .05 alpha level to detect a medium-sized effect ($f = .20$; cf. Cohen,

1988). Effect sizes in previous research have ranged from $\eta^2 = 0.08$ (small effect) to $\eta^2 = 0.86$ (large effect), with most falling in the medium to large range. Effect sizes for studies assessing the relationship between a pupil dilation parameter and anxiety average $\eta^2 = 0.21$ (medium-large effect).

2.2.2 Preliminary Analyses

As the first step, I separated feedback face images into four conditions—high angry, high happy, low angry, and low happy—with faces of 10% and 20% emotional intensity categorized as "low" and faces of 30%, 40%, and 50% emotional intensities categorized as "high". This approach to grouping emotional faces maximized power, given the small number of trials at each intensity level, for each emotion, for each individual. Due to an insufficient number of trials, I dropped all 0%, or "neutral" feedback face trials. Pupil diameter averages for each of the four conditions served as variables in all subsequent analyses.

Prior pupillary dilation research has yielded minimal evidence of statistically significant gender differences (Siegle et al., 2003; Partala & Surakka, 2003); however, this body of research suggests that age should be considered as a covariate of potential importance (Silk, Siegle, Whalen, Ostapenko, Ladouceur, & Dahl, 2009). The pupil continues to grow throughout childhood and adolescence and has been documented to reach its peak size between the ages of 6 and 20 (Boev et al., 2005; Kohnen, Zubcov, & Kohnen, 2004; MacLachlan & Howland, 2002). Larger pupils allow for a broader range of reactivity, introducing potential confounding information in studies focused on children and adolescents. The average age of our sample was above this age range; however, some participants were between 18 and 20 years old.

I thus conducted bivariate correlations among age, LSAS-SR Avoidance and Fear subscales, Total LSAS-SR, age, gender, and pupil diameter in response to low and high happy

and angry faces at 0.5 seconds, 1 second, and averaged across the significant time window described below (See Figure 2.2). I used the results of these bivariate correlations to inform decisions about potential covariates to include in analyses. I also conducted t-tests to compare scores on all measures between men and women to evaluate the need to covary gender.

Next, I examined whether pupil diameter responses to the feedback faces differed according to face emotion or intensity. For this, I utilized the Pupil Toolkit. The Pupil Toolkit is a collection of MATLAB code that Dr. Greg Siegle developed for pre-processing pupillary data and extracting critical variables for analyses. These variables include absolute diameter, change in diameter, and time-course data. For the present study, I extracted average pupil diameter between 0.45 seconds and 2.23 seconds post stimulus presentation. I focused on this time frame based on visual inspection of a graph of dilation changes over time. As shown in Figure 2.2, dilation variability among feedback face conditions occurred during the selected window. Moreover, data become progressively sparser following the end of this window, because participants typically advanced to the next trial between 2.23 and 4 seconds after trial onset.

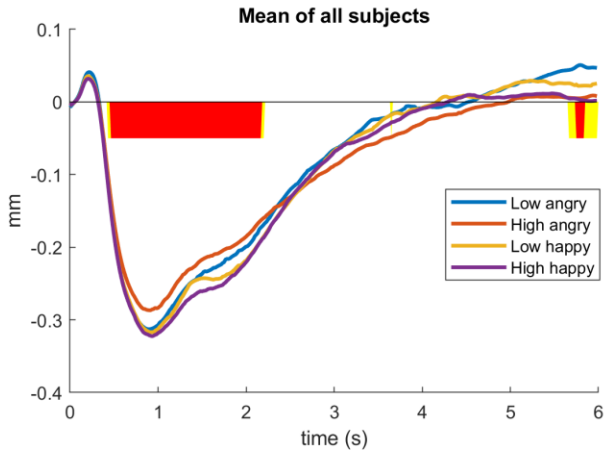

Figure 2.2 Overall Pupillary Patterns to Low and High Happy and Angry Faces

Using the data gathered at each sampling point, I generated values reflecting peak dilation, dilation latency, and sustained dilation duration for each participant. Because presentation of bright feedback faces following a dark screen elicited a consistent light reflex (large decrease in pupil size reflecting pupillary constriction when light falls on the retina), I was not able to accurately determine a meaningful "peak" in dilation as proposed. Thus, rather than defining peak dilation as the largest pupil diameter in a time window following stimulus onset, I operationally defined peak dilation as the largest absolute change in pupil diameter following stimulus onset. In the present sample, absolute diameter change was maximal at 1 second post-stimulus onset across participants (See Figures 2.2, 2.3, and 2.4). Therefore, pupil diameter at 1 second post-stimulus onset served as my measure of peak dilation.

Similarly, I had proposed that I would define sustained dilation as the length of time that the peak dilation is sustained. However, to align with changes in my definition of peak dilation, I instead determined sustained dilation based on the procedure described in Siegle et al. (2003). Specifically, I calculated the average pupil diameter during a "sustained" time window from the time at which the largest absolute change in pupil diameter occurred (i.e., 1 second) to the end of the time window in which variability across conditions was evident (i.e., 2.5 seconds), yielding

an estimate of average pupil size during the time window of 1 second to 2.5 seconds post-stimulus onset as my measure of sustained dilation.

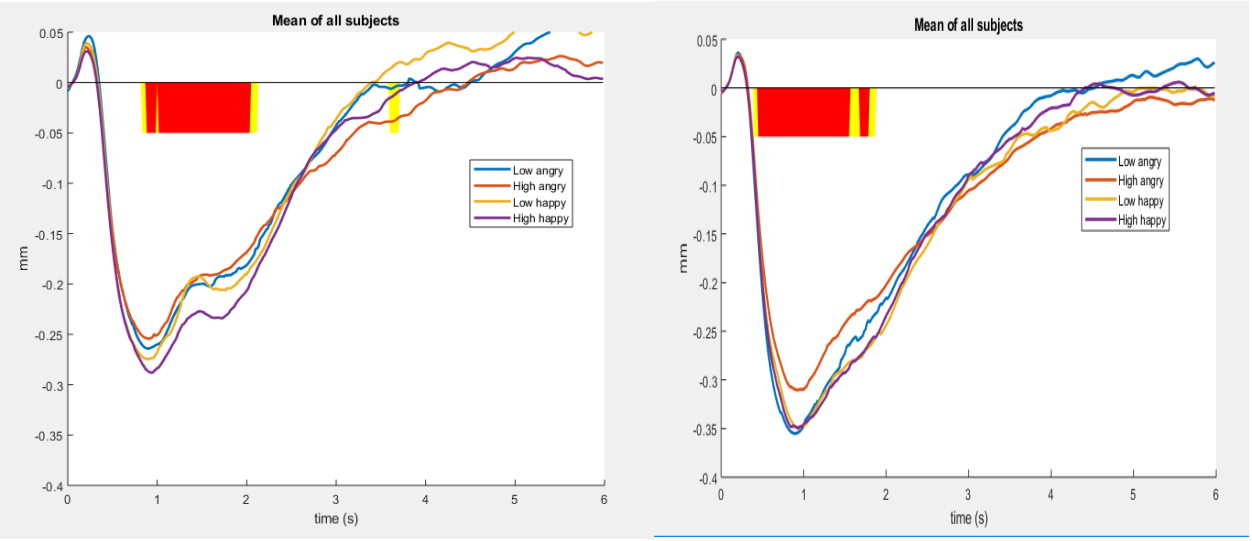

Figure 2.3 Pupillary Response Patterns to Low and High Happy and Angry Faces for Low (left) and High (right) Socially Anxious Individuals

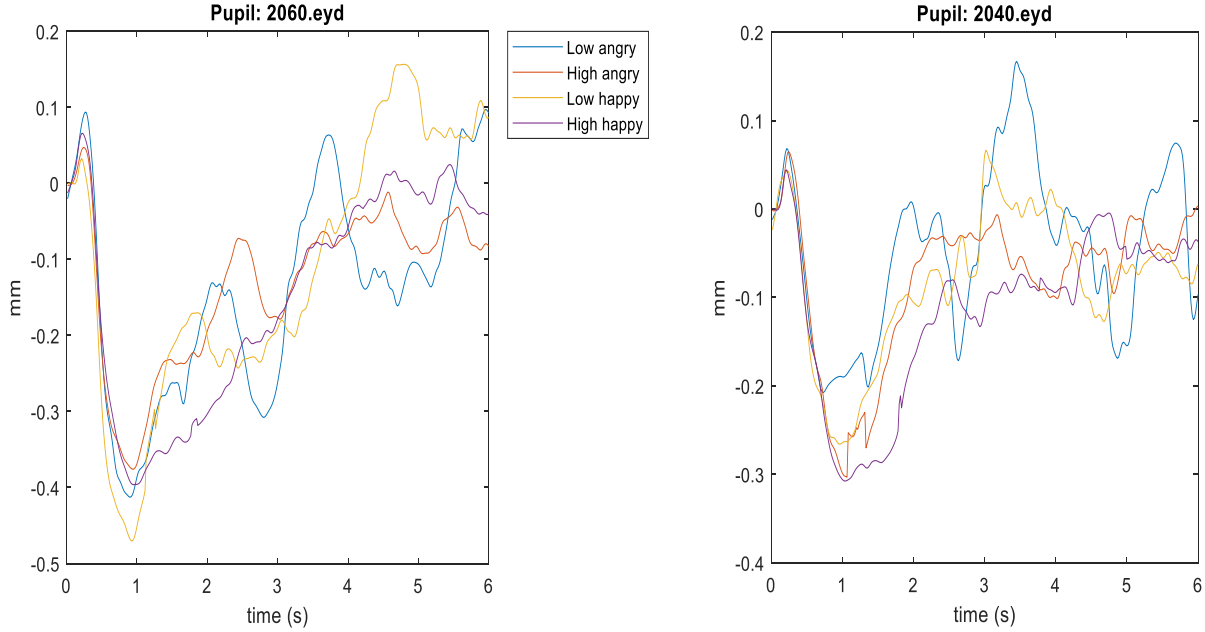

Figure 2.4 Pupillary Patterns to Low/High Happy/Angry Faces for Two Subjects

Finally, I had proposed that I would define peak latency as the amount of time between stimulus onset and peak dilation. However, in light of the necessary changes in my definition of peak dilation, I was unable to generate this variable. I thus instead assessed pupil size at 0.5 seconds after stimulus onset, which, based on visual inspection, is when pupillary patterns in response to each feedback face condition showed the largest divergence across individuals, as well as between low and high SA groups (See Figures 2.3 and 2.4). In other words, for each feedback face condition, individuals began to show significant differences in pupil diameter beginning at 0.5 seconds following the stimulus onset (depicted by the start of the red bar in Figure 2.2). Therefore, given my research question –whether or not individuals higher in SA would display significantly different, immediate attention to negative stimuli (measured by latency) compared to those lower in SA—it is informative to assess the difference in pupil size at 0.5 seconds post-stimulus onset, when differences in pupillary response patterns to the feedback face conditions began to emerge. Thus, for analyses assessing differences in dilation latency, I utilized pupil size at 0.5 seconds post-stimulus onset.

2.2.3 Analyses for Specific Aim 1

The first hypothesis of Aim 1 was that higher peak dilation would be associated with a higher level of SA. Since I had inadequate data from "neutral" trials to include them in analyses, I conducted a 2 (Anxiety group) x 2 (High intensity face emotion) repeated measures ANOVA. LSAS-SR Total score split at the 50th percentile (creating low and high SA groups) served as the between-subjects factor, and pupil diameter in response to high intensity valence (high angry and high happy) at 1 second post-stimulus onset served as the within-subject factor. I also tested two separate linear regression models to assess the association between total LSAS-SR score and

pupil diameter at 1 second post-stimulus onset in response to high angry and high happy face conditions separately.

The second hypothesis of Aim 1 was that level of face intensity (50% happy-50% angry) would predict peak dilation, such that the relationship between peak dilation and SA would be stronger for lower (low angry and low happy) compared to higher (high angry and high happy) face intensities. To test this hypothesis, I conduced a linear regression analysis with Total LSAS-SR as the dependent variable and average pupil diameter at 1 second post-stimulus onset in response to each feedback face condition as the independent variables. Since age was not correlated with Total LSAS-SR (See Table 3.3) and no gender differences emerged for Total LSAS-SR (See Table 3.4), I did not include age or gender as predictors in subsequent models.

2.2.4 Analyses for Specific Aim 2

The first hypothesis of Aim 2 was that longer sustained dilation would be associated with a higher level of SA. To assess this, I conducted analyses using window means during the "sustained" dilation period (i.e., 1 second to 2.5 seconds following stimulus onset). I conducted a 2 (Anxiety group) x 2 (High intensity face emotion) repeated measures ANOVA with LSAS-SR Total score split at the 50th percentile creating low and high SA groups as the between-subjects factor and pupil diameter in response to high intensity valence (high angry and high happy) during the "sustained" time window as the within-subject factor. I also tested two regression models to assess the association between total LSAS-SR score and average pupil dilation during the "sustained" time window for each of the two conditions (high happy and high angry).

The second hypothesis for Aim 2 was that level of face intensity (50% happy-50% angry) would predict sustained dilation, such that the relationship between sustained dilation and SA would be stronger for lower (low angry and low happy) compared to higher (high angry and high

happy) face intensities. In order to test this hypothesis, I conducted a linear regression analysis where SA served as the dependent variable and pupil dilation duration in response to each face condition served as the independent variables.

2.2.5 Analyses for Specific Aim 3

The first hypothesis of Aim 3 was that shorter dilation latency would be associated with a higher level of SA. Given my modified tests to address the question of whether or not individuals higher in SA would exhibit significantly different, immediate attention to negative stimuli (measured by latency) compared to those lower in SA, I used the variable for pupil diameter at 0.5 seconds post-stimulus onset when the pupillary response pattern changes for each condition. I conducted a 2 (Anxiety group) x 2 (High intensity face emotions) repeated measures ANOVA with social anxiety level (LSAS-SR Total score split at the 50^{th} percentile) as the between-subjects factor and pupil diameter in response to high intensity valence (high angry and high happy) at 0.5 seconds post-stimulus onset as the within-subjects factor.

The second hypothesis of Aim 3 was that level of face intensity (50% happy-50% angry) would predict dilation latency, such that the relationship between dilation latency and SA would be stronger for lower (low angry and low happy) compared to higher (high angry and high happy) face intensities. To test this hypothesis, I conducted a linear regression with Total LSAS-SR as the dependent variable and average pupil diameter at 0.5 seconds post-stimulus onset in response to each feedback face condition (high angry, high happy, low, angry, low happy) as independent variables.

3 RESULTS

3.1 Preprocessing Steps

After cleaning the pupillary dilation data according to documented procedures (e.g., Siegle, Granholm, Ingram, & Matt, 2001; Siegle, Steinhauer, Carter, Ramel, & Thase, 2003), I excluded participants (n = 4) with unreadable behavioral or pupillary data files from analyses. Included participants' demographics are presented in Table 3.1 below.

Table 3.1 Included Participant Characteristics

N (# of participants)	55
Sex (% Male)	16.4%
Race (% White)	27.3%
(% Black/African American)	58.2%
(% Asian/Asian American)	7.3%
Ethnicity (% Hispanic or Latino)	7.3%
Age at examination (SD)	20.77 (3.76)

3.2 Preliminary Analyses

I conducted a one-way repeated measures ANOVA to compare mean pupil diameters in response to high angry, low angry, high happy, and low happy feedback face conditions. Results indicated a significant omnibus effect of feedback face condition, Wilks' Lambda = .705, $F(3, 52) = 7.244$, $p < .001$, $\eta_p^2 = 0.053$. Post hoc comparisons using paired samples t-tests (See Table 3.2) indicated a significant difference between the high angry (M = -.22, SD = .13) and high happy (M = -.26, SD = .14) conditions, $t(54) = 4.74$, $p < .001$, $\eta_p^2 = 0.294$, such that pupil diameter was larger in response to high angry than high happy faces. No other t-tests yielded evidence of significant differences (all p's > .05).

Table 3.2 Paired Samples T-Tests for Preliminary Analyses

		Mean	SD	*t*	df	*p*
Pair 1	High Angry – Low Angry	0.019	0.09	1.522	54	0.134
Pair 2	High Angry – Low Happy	0.025	0.096	1.969	54	0.054
Pair 3	High Angry – High Happy	0.035	0.055	4.744	54	<0.001**
Pair 4	High Happy – Low Happy	-0.009	0.091	-0.780	54	0.439

*p<.05, ** p<.01

I next assessed the relationship between SA and pupil diameter in response to feedback faces of varying intensities. I conducted bivariate correlations among age, LSAS-SR Total score, Avoidance and Fear subscale scores, and average pupil diameter in response to each face feedback condition during the time window that encompassed 0.45 seconds to 2.23 seconds following stimulus onset. Age was not significantly associated with SA or any of the pupil diameter response variables (See Table 3.3), and therefore was not included as a covariate in subsequent analyses.

Table 3.3 Correlations with Age

	1	2	3	4	5	6	7
1. Age	1						
2. Total LSAS	-0.055	1					
3. LSAS-SR Fear	-0.049	.915**	1				
4. LSAS-SR Avoidance	-0.052	.925**	.694**	1			
5. Low Angry	0.088	-0.136	-0.07	-0.177	1		
6. High Angry	-0.014	-0.071	-0.025	-0.104	.838**	1	
7. Low Happy	0.081	-0.189	-0.121	-0.225	.781**	.779**	1
8. High Happy	0.016	-0.07	0.017	-0.142	.834**	.924**	.810*

*p<.05, ** p<.01

I also conducted t-tests to compare all pupil diameter response variables between men and women. No significant group differences emerged (See Table 3.4), and therefore, gender was not included as a covariate in subsequent analyses. Age and gender were the only two participant characteristics that I had identified a priori as potential covariates.

Table 3.4 Gender Pupil Dilation Means and T-Tests

Condition	Gender	*N*	*Mean*	*Std. Dev*	*Std. Error Mean*	*t*	*df*	*p*
LA	Female	46	-0.23	0.161	0.024	0.750	53	0.457
	Male	9	-0.28	0.193	0.064			
HA	Female	46	-0.23	0.131	0.019	-0.293	53	0.771
	Male	9	-0.21	0.153	0.051			
LH	Female	46	-0.24	0.138	0.02	1.364	53	0.178
	Male	9	-0.31	0.205	0.068			
HH	Female	46	-0.25	0.142	0.021	0.729	53	0.469
	Male	9	-0.29	0.156	0.052			

*p<.05, ** p<.01
Note: HA = high angry faces; HH = high happy faces; LA = low angry faces; LH = low happy faces.

3.3 Hypothesis Tests

3.3.1 Results for Specific Aim 1

All assumptions for repeated measures ANOVA, including sphericity, were met. Results of the first 2 (Anxiety group) x 2 (High intensity face emotion) repeated measures ANOVA, yielded evidence of a significant difference between High Angry and High Happy conditions, Wilks' Lambda = 0.718, $F(1, 53) = 20.770$, $p < 0.001$, $\eta_p^2 = 0.282$. No significant differences between anxiety groups emerged ($F(1, 53) = 2.412$, $p = 0.126$, $\eta_p^2 = 0.044$), and the interaction term was also non-significant, Wilks' Lambda = .998, $F(1, 53) = 0.097$, $p = .757$, $\eta_p^2 = 0.002$ (See Table 3.5), suggesting that SA and high intensity face emotion type did not interact to predict peak pupil dilation. Results of linear regression analyses assessing the association

between total LSAS-SR score and pupil diameter at 1 second post-stimulus onset in response to high angry, $F(1, 53) = .577$, $p = .451$, $\beta = -0.104$, $t = -0.759$, and high happy, $F(1, 53) = 0.434$, $p = .513$, $\beta = -0.090$, $t = -0.659$), conditions also yielded non-significant results.

Table 3.5 Repeated Measures ANOVA for Specific Aim 1

Tests of Between-Subjects Effects				
	Type III Sum of Squares	*F*	*Error df*	*p*
Anxiety Group	0.104	2.412	53	0.126
Tests of Within-Subject Effects				
	Wilks' Lambda	*F*	*Error df*	*p*
Emotion	0.718	20.770	53	0.000**
Emotion*Anxiety Group	0.998	0.097	53	0.757

*$p<.05$, ** $p<.01$
Note: Anxiety Group = LSAS-SR Total score split at the 50th percentile

Results of the linear regression with Total LSAS-SR as the dependent variable and average pupil diameter at 1 second post-stimulus onset (when the "peak" occurred) in response to each feedback face condition (high angry, high happy, low, angry, low happy) as independent variables, indicated an overall model that was non-significant, $F(4, 50)=0.704$, $p=.593$. This finding precluded examination of the effects of individual conditions (See Table 3.6).

Table 3.6 Regression for Specific Aim 1

	LSAS-SR Total			
	B	*Std. Error*	*t*	*p*
PPD in response to LA	-0.250	37.722	-0.780	0.439
PPD in response to HA	0.077	65.034	0.174	0.863
PPD in response to LH	-0.239	38.233	-0.850	0.399
PPD in response to HH	0.252	58.853	0.590	0.558
R^2	0.053			
F	0.593			

*$p < .05$; **$p < .01$
Note: PPD = (Peak Pupil Diameter) Average pupil diameter at 1 second post-stimulus onset; HA = high angry faces; HH = high happy faces; LA = low angry faces; LH = low happy faces.

3.3.2 Results for Specific Aim 2

Results of the first 2 (Anxiety group) x 2 (High intensity face emotion) repeated measures ANOVA, yielded evidence of a significant difference between High Angry and High Happy conditions during the sustained time window, Wilks' Lambda = .770, $F(1, 53)=15.861$, $p<.001$, $\eta_p^2= 0.230$. However, there was neither a significant effect of anxiety group, $F(1, 53)=1.479$, $p=0.229$, $\eta_p^2= 0.027$, nor was there a significant interaction effect, Wilks' Lambda = 1.00, $F(1, 53)=.015$, $p=.902$, $\eta_p^2= 0.000$ (See Table 3.7). Results of linear regression analyses assessing the association between total LSAS-SR score and pupil diameter during the sustained time window post-stimulus onset in response to high angry ($F(1, 53) = 0.179$, $p = .674$, $\beta = -0.058$, $t = -0.423$) and high happy ($F(1, 53) = 0.143$, $p = .701$, $\beta = -0.052$, $t = -0.378$), conditions were also non-significant.

Table 3.7 Repeated Measures ANOVA for Specific Aim 2

Tests of Between-Subjects Effects				
	Type III Sum of Squares	*F*	*Error df*	*p*
Anxiety Group	0.063	1.479	53	0.229
Tests of Within-Subject Effects				
	Wilks' Lambda	*F*	*Error df*	*p*
Emotion	0.770	15.861	53	0.000**
Emotion*Anxiety Group	1.000	0.015	53	0.902

*p<.05, ** p<.01
Note: Anxiety Group = LSAS-SR Total score split at the 50th percentile

Results of the linear regression analysis indicate that the overall model was not significant, $F(4, 50)=0.809$, $p=.525$ (See Table 3.8), and therefore the model cannot be interpreted.

Table 3.8 Regression for Specific Aim 2

	LSAS-SR Total			
	B	*Std. Error*	*t*	*p*
SusPD in response to HA	0.055	54.934	.148	.883
SusPD in response to HH	0.301	54.090	.765	.448
SusPD in response to LA	-0.119	34.260	-.416	.679
SusPD in response to LH	-0.373	31.893	-1.527	.133
R^2	0.061			
F	0.809			

*p<.05; **p<.01
Note. SusPD = average pupil diameter from 1second to 2.5 seconds post-stimulus onset; HA = high angry faces; HH = high happy faces; LA = low angry faces; LH = low happy faces.

3.3.3 Results for Specific Aim 3

Results of the first 2 (Anxiety group) x 2 (High intensity face emotion) repeated measures ANOVA, yielded significant difference between High Angry and High Happy conditions

(Wilks' Lambda = .875, $F(1, 53) = 7.601$, $p < .01$, $\eta_p^2 = 0.125$). However, there was neither a significant effect of anxiety group ($F(1, 53) = 1.996$ $p = 0.164$, $\eta_p^2 = 0.036$), nor was there a significant interaction effect (Wilks' Lambda = .995, $F(1, 53) = .276$, $p = .602$, $\eta_p^2 = 0.005$), suggesting that SA and high intensity face emotion type did not interact to predict dilation latency. Results of linear regression analyses assessing the association between total LSAS-SR score and pupil diameter at 1 second post-stimulus onset in response to high angry, ($F(1, 53) = 2.525$, $p = .118$, $\beta = -.189$, $t = -1.589$), and high happy ($F(1, 53) = 1.959$, $p = .167$, $\beta = -0.213$, $t = -1.400$), conditions were also not significant.

Table 3.9 Repeated Measures ANOVA for Specific Aim 3

Tests of Between-Subjects Effects				
	Type III Sum of Squares	*F*	*Error df*	*p*
Anxiety Group	0.018	1.996	53	0.164
Tests of Within-Subject Effects				
	Wilks' Lambda	*F*	*Error df*	*p*
Emotion	0.875	7.601	53	0.008**
Emotion*Anxiety Group	0.995	0.276	53	0.602

*$p<.05$, ** $p<.01$
Note. Anxiety Group = LSAS-SR Total score split at the 50th percentile

Results of the linear regression showed that the overall model was not significant ($F(4,50)=2.067$, $p=.099$), and therefore the model cannot be interpreted. Although individual effects should not be interpreted in the context of a non-significant model, it is worth noting, for the purpose of informing future hypothesis tests, that the strongest association present was between Total LSAS-SR and pupil diameter in response to Low Angry faces. Further, the direction of the association was negative, suggesting that for low angry faces only, high SA was associated with lower pupil diameter (See Table 3.10).

Table 3.10 Regression for Specific Aim 3

	LSAS-SR Total			
	B	*Std. Error*	*t*	*p*
PDL in response to HA	0.231	89.399	0.804	.425
PDL in response to LA	-0.464	51.377	-2.252	.029*
PDL in response to HH	-0.059	81.069	-0.221	.826
PDL in response to LH	-0.032	59.053	-0.148	.883
R^2	0.142			
F	2.067			

*p<.05; **p<.01
Note. PDL = (Pupil Diameter Latency) Average pupil diameter at 0.5 seconds post-stimulus onset; HA = high angry faces; HH = high happy faces; LA = low angry faces; LH = low happy faces.

4 DISCUSSION

The present study was designed to assess if anxiety, particularly SA, is associated with an exaggerated pupillary response to threat cues. Using archival data, I examined associations between self-reported SA and patterns of pupillary response to feedback faces that were morphed in intensity from happy to neutral to angry. I hypothesized that, relative to individuals who endorsed low levels of SA, individuals high in SA would display larger peak diameter, shorter dilation latency, and longer dilation duration in response to faces that appeared subtly threatening or neutral. I aimed to extend the existing literature by embedding faces in the context of evaluative feedback, which individuals experiencing SA are particularly sensitive to (Rapee & Heimberg, 1997; Hofmann, 2007), and by assessing three different measures of pupil dilation in a sample that provides more power than has been typical in this literature.

Results revealed that across individuals, regardless of their levels of SA, pupil diameter was significantly larger in response to intensely angry than intensely happy faces. Results of our hypothesis tests; however, revealed no significant effects of anxiety group on pupil diameter at 0.5 seconds or 1 second post-stimulus onset, nor were there anxiety-related differences evident

during the sustained dilation window of 1.5 to 2.5 seconds post-stimulus onset. Nevertheless, these findings add to the existing body of research on associations between pupil diameter and anxiety and reinforce the idea that such associations may be less robust or consistent than those observed in individuals with other psychological conditions, such as depression or schizophrenia.

Moreover, the findings suggest the need to consider a range of potential moderating factors in future studies exploring pupillary dilation in the context of anxiety. For example, there is some evidence to suggest that, among individuals high in SA, a subset preferentially avoids, rather than attends to, threatening cues (Price, Tone, & Anderson, 2011; Waters, Mogg, & Bradley, 2012). Pupil diameter measures might differentially reflect these subtypes, warranting the assessment of eye-gaze as a moderating variable. Further, faces that violate expectancies have been shown to affect pupillary dilation latency and size (Proulx, Sleegers, Tritt, 2017), suggesting the potential need to control for feedback expectancy violation in similar task designs among anxious individuals.

4.1 Associations Between SA and Pupil Diameter

Tests of hypotheses that SA would be associated with elevated peak dilation, longer sustained dilation, and shorter latency in response to high angry and high happy faces yielded nonsignificant results. These findings align with those from the one other study to date that assessed associations between anxiety and peak diameter in response to emotional faces (Hepsomali et al., 2017). In Hepsomali and colleagues' paper, although high anxious participants showed a slowed and exaggerated pupillary response to faces in general, relative to low anxious individuals, anxiety did not interact with stimulus emotion to predict peak dilation response. In the present study, individuals higher in SA showed a diminished pupillary response to faces in general at 0.5 seconds post-stimulus onset, relative to individuals lower in SA (r = -.278; p <

.05). When face intensity was considered, this negative association between pupil diameter and SA at 0.5 seconds post-stimulus onset remained significant for low angry faces only (r = -.357; p < .01). While Hepsomali and colleagues reported an exaggerated pupillary response to faces in general, our results suggest a diminished pupillary response to faces in general, which is largely driven by the pupillary response to low angry faces.

Of note, the range of SA in our sample was relatively restricted. The mean LSAS-SR score for the sample (51.87, SD = 22.78) was below the clinical cutoff of 60 points, and only 21 participants obtained scores that exceeded this benchmark. The average pupil diameter in response to faces in general across the significant time window (0.45 to 2.23 seconds) for individuals below the clinical cutoff was larger (-0.22 mm) than that of individuals above the clinical cutoff (-0.28 mm). It is possible that predicted group differences would have been evident in a sample that better captured the full range, particularly the upper extremes, of the range of SA severity. To date, only a few studies have compared pupillary responses among individuals with clinically significant anxiety to those of people without high anxiety levels (Price et al., 2012; Bakes, Bradshaw, Szabadi, 1990). Both studies found significantly different pupillary responses between groups; thus the comparison of pupil diameter group differences between individuals below and above clinical cutoffs may be more likely to permit detection of anxiety-related effects.

It is also possible that, in line with both our and Hepsomali et al.'s findings, intensely emotional faces, regardless of their valence, elicit uniformly exaggerated responses in most people. If this is the case, then anxiety might be more tightly associated with inefficient regulation of a strong, but normative, reaction to intense, emotionally-evocative stimuli than with the reaction itself. Recent work suggests that cognitive control of the pupillary reflex might be

functional and serve to filter visual information, shape visual perceptions, and produce an adaptive motor response (Ebitz & Moore, 2018). It is therefore possible that extremely angry faces, that might suggest the presence of threat (Mogg et al., 2004), evoke similarly exaggerated responses in most people owing, at least in part, to cognitive control of the pupillary reflex that serves to optimally evaluate such threat.

An additional possibility that the present findings, taken together with Hepsomali and colleagues' results raise, is that the strongest associations between anxiety and pupillary dilation to salient emotional expressions might emerge when those expressions are of low intensity, and thus ambiguous with regard to whether they convey positive or negative information. Cognitive models of SA provide a framework for this idea, by proposing that socially anxious individuals are prone to interpret ambiguous social events negatively and to catastrophize about the consequences that social cues perceived as negative might signal (for a review, see; Clark & McManus, 2002). Moreover, a solid empirical base supports the idea that social anxiety is associated with negatively biased interpretation of ambiguous cues, such as neutral faces (e.g., Constans, Penn, Ihen, & Hope, 1999; Gutiérrez-García & Calvo, 2017; Yoon & Zinbarg, 2008).

Contrary to my predictions, however, the relationships between SA and peak dilation, sustained dilation, and dilation latency were not significantly stronger for low-intensity than for high-intensity feedback faces. Prior work examining responses to neutral or low-intensity emotional images in healthy adults has shown that pleasant and unpleasant images (Bradley, Miccoli, Escrig, Lang, 2013) and sounds (Partala, Jokiniemi, Surakka, 2000) evoke increased pupil dilation compared to neutral images and sounds, respectively. Similarly, it seems plausible that, despite potential negative interpretation of low-intensity stimuli, socially anxious

individuals evaluate these stimuli within a normative time frame (similar pupillary reflex time-course) and subsequently allocate attentional resources toward more threatening cues (Mogg & Bradley, 1998; Öhman, 1996; Williams, Watts, MacLeod, & Matthews, 1997).

There is also some evidence that the degree to which faces violate expectancies affects pupillary dilation latency and size more strongly than do emotional expressions (Proulx, Sleegers, Tritt, 2017). Therefore, it is possible that high compared to low anxious individuals might display significantly different pupillary responses when performance expectancy is violated by the feedback face. For example, low anxious individuals might believe they performed well and expect a happy face, but instead receive an angry face; high anxious individuals, in contrast, might instead expect negative feedback and be surprised by a positive response. This possibility can be explored in the future by assessing trials where participants rated their performance poorly and received a happy feedback face or rated their performance positively and received an angry feedback face.

At least two methodological issues warrant consideration in efforts to make sense of our findings. First, participants were not instructed to look at the feedback faces during the task. Thus, individuals in our sample varied according to how closely they attended to the faces, which might have introduced variability in pupil diameter response patterns. There is some evidence that, among individuals high in SA, a subset preferentially avoids, rather than attends to, threatening cues (Price, Tone, & Anderson, 2011; Waters, Mogg, & Bradley, 2012). Pupillary dilation patterns could differ between anxious individuals who are attentionally avoidant and those who are attentionally vigilant. For example, avoidance of potentially threatening images might lower physiological arousal, and as a result, pupil diameter among this sample might be lower than it is for those who attend to the threatening image and consequently

experience an increase in physiological arousal. It would be beneficial to assess this possibility in future studies via analysis of concurrent eye-tracking data that capture gaze duration at salient stimuli.

A second methodological issue that warrants attention is the window of time (1 to 2.5 seconds post-stimulus) within which the pupillary response was measured. The decision to focus on this period may have prevented analysis of information regarding sustained information processing, which could unfold over several seconds following the feedback stimulus. If this is the case, it could be useful to examine pupillary response measures during a longer window of time. Indeed, the two studies that have assessed sustained pupil diameter among depressed (Siegle et al., 2003) and anxious (Price et al., 2013) individuals noted differences in sustained pupil diameter beginning at 4 seconds and extending to 10 seconds post-stimulus onset. Therefore, it is possible that a difference in sustained, heightened pupil diameter in response to extreme happy and angry feedback faces between low and high socially anxious individuals does exist in our sample, but I failed to detect it due to my focus on a relatively short response time window. Future research might benefit from including longer inter-stimulus intervals and fixed-duration response windows that prevent participants from advancing to the next trial before several seconds have elapsed in the study design to assess this possibility.

Finally, tests of the hypothesis that SA would be associated with shorter latency in response to high angry and high happy faces yielded nonsignificant results. Unexpectedly, the association between SA and pupil diameter at 0.5 seconds was strongest in response to Low Angry faces, such that higher SA was associated with smaller pupil diameter. One recent study investigating pupillary reactivity to and eye contact with emotional faces among children with SAD, mixed anxiety disorders, and healthy controls, found evidence of reduced pupil dilation in

response to happy and angry faces in girls with SAD compared to girls with mixed anxiety disorders and healthy controls (Keil, Hepach, Vierrath, Caffier, & Tuschen-Caffier, 2018). Boys with SAD, in contrast, showed reduced pupil dilation to neutral faces compared to healthy controls. Keil and colleagues noted that, although the pattern of blunted pupillary reactivity that they observed aligns poorly with cognitive models of SAD, it is consistent with results from studies that have reported blunted autonomic reactivity to social stress among children with SAD (Schmitz, Krämer, Tuschen-Caffier, Heinrichs, & Blechert, 2011; Schmitz, Tuschen-Caffier, Wilhelm, & Blechert, 2013).

Of note, eye tracking results revealed that children with SAD in Keil and colleagues' study initially fixated more briefly on the eye regions of all faces than did healthy controls. Taken together with the study's pupillary dilation data, this finding raises the possibility that at least among children with SAD, avoidance of social cues dampens normative autonomic responses to those cues. Findings from one study of healthy adults found decreased pupil dilation to be linked to increased visual avoidance of emotional scenes (Bebko, Franconeri, Ochsner, & Chiao, 2011), suggesting that blunted pupillary reactivity might reflect disengagement from a threatening cue, but research has yet to examine whether SA modulates the association. It is an open question whether participants in the present study who endorsed high levels of SA may also have avoided looking at the facial images; there may be value, however, in gathering eye-tracking and pupillary response data concurrently in studies of anxious individuals.

4.2 Overall Pupillary Responses to Low and High Angry and Happy Faces

Results of analyses aimed at characterizing pupillary responses to low and high angry and happy faces, regardless of participants' levels of SA, showed that, for the full sample, pupil

diameter was largest in response to high angry faces and smallest in response to high happy faces. This finding suggests that both the intensity (low vs. high) and the valence (angry vs. happy) of viewed facial expressions modulated viewers' physiological arousal. Previous literature regarding pupil diameter responses to different emotional valences has yielded mixed results. Specifically, whereas some studies have shown no differences in pupil diameters in response to positive and negative images (Partala & Surakka, 2003; Kudinova, Burkhouse, Siegle, Owens, Woody, Gibb, 2016; Bradley, Miccoli, Escrig, & Lang, 2013), others have found larger pupil size in response to negative than to positive stimuli (Kret et al., 2013; Hepsomali et al., 2017).

Hepsomali and colleagues' (2017) findings raise an additional possibility. In this study, angry faces elicited a larger pupillary response than did happy faces (Hepsomali et al., 2017), The authors suggest that this pattern may have emerged because people perceive extreme angry faces as threatening (Fox, Lester, Russo, Bowles, Pichler, & Dutton, 2000), and those faces therefore elicit a large physiological response. Clearly non-threatening faces, such as those with intensely happy expressions, in contrast, convey minimal threat and therefore produce smaller physiological reactions.

The present study helps clarify the impact of emotional valence and intensity on physiological responses, in the context of personally-relevant feedback faces. Specifically, while all emotional cues elicit a physiological response, our data do not support the idea that such physiological responses occur independently of valence (Bradley et al., 2008), suggesting that angry or threatening faces might be prioritized in the context of other emotional faces.

4.3 Strengths and Limitations

The present study has several strengths. First, it extends our knowledge about pupillary dilation profiles in the context of anxiety by examining patterns associated specifically with SA. Second, unlike many prior studies, it focused on the pupillary response time-series as a whole, rather than focusing simply on individual overall or peak dilation parameters. Third, the present study utilized a task that assessed pupil diameter responses to morphed facial intensities in the context of feedback, which allows for numerous questions to be answered and moderating variables to be explored (face intensity, feedback expectancy violation, etc.). Future research may build from this work and more systematically assess each potential moderator (e.g., presence vs. absence of feedback, varying levels of SA). Alternatively, such a task might be used as a baseline or comparison for different anxious populations or face stimuli (e.g., sad).

Several weaknesses of the proposed study also warrant mention. First, the sample size, though sufficient to detect a moderately sized effect, was inadequate to detect true effects if those are small. Second, the sample was not drawn from a clinical population; therefore, the cutoff used to delineate low and high SA is statistically (50^{th} %ile), rather than diagnostically, based. Use of a diagnostic cutoff would allow our results to more readily generalize to clinical populations. However, assessing a wide range of symptom severity rather than assessing group differences (e.g. clinical vs. healthy) is likely more ecologically valid and better representative of the population at large. Additionally, the average level of SA endorsed by the present sample falls below the 60-point clinical cut-off, suggesting less severe SA pathology in our sample than in a clinically or diagnostically significant SA sample. This lack of variability at the clinically significant range of SA within our sample might have prevented us from detecting a difference that might exist between those above and below a clinical cut-off for SAD. Further, the lack of a

comparison group with participants who endorse symptoms of different internalizing problems makes it difficult to be certain that the pupillary waveform found is one specific to SA, rather than reflective of general negative affect or distress. Future research might benefit from assessing a larger sample size that includes a broad range of anxiety severity, including a clinically significant representative population.

4.4 Conclusions and Future Directions

Our findings did not support our hypotheses regarding associations between SA and peak pupillary dilation, sustained dilation, or latency in response to emotional faces that were providing feedback to participants regarding their task performance. Additionally, contrary to hypotheses, a diminished pupillary response to Low Angry faces was evident among individuals who reported higher SA. These findings, taken together, might suggest that high-intensity angry faces evoke similar responses among individuals reporting low and high SA, given the valence of the potential threat, and that blunted pupillary reactivity among individuals reporting higher SA might reflect disengagement from a threatening cue. Finally, across the sample, pupil diameter was largest in response to high angry faces and smallest in response to high happy faces, suggesting the importance of both intensity (low vs. high) and valence (angry vs. happy) of facial expressions in elicited physiological arousal.

The present findings help to lay groundwork for further research examining pupil dilation among anxious individuals. Perhaps most importantly, they suggest a number of methodological shifts that might be helpful for researchers to consider. First, examination of pupillary reactions using multiple parameters over the course of the response to a stimulus may be more informative than focusing on measures of individual parameters in isolation. In addition, there may be value in work examining pupillary responses within putative subgroups of SA, particularly proposed

vigilant and avoidant types (Price et al., 2011). Research on pupillary dilation in anxious individuals might also benefit from the inclusion of participants who meet clinical criteria for social or general anxiety disorders, along with those whose symptoms are milder. Additionally, comparison groups of individuals experiencing different internalizing problems like depression might help to isolate responses specific to anxiety rather than emotion dysregulation in general.

With regard to study design, future studies should use concurrent eye-tracking and pupil diameter measures to simultaneously measure eye gaze direction and duration as well as pupillary response patterns. Concurrent measurement might allow us to detect trends in pupil diameter that can be explained by eye gaze patterns, and vice-versa. It may also be helpful to examine responses during an extended reaction-time window, which was not possible in the present study. Additionally, research assessing pre-stimulus or baseline pupillary patterns among high anxious compared to low anxious individuals might provide insight into the levels of arousal while preparing for a cue, as well as any differences in resting pupil diameter. Finally, the neural mechanisms behind pupillary responses to threat remain unclear and would benefit from further investigation. For example, combining measurement of brain activation via functional Magnetic Resonance Imaging (fMRI) and pupil diameter may yield informative results. Pupil diameter remains a parsimonious and inexpensive measure of cognitive and emotional load, and optimizing its utility will be a benefit to future work.

REFERENCES

Aboyoun, D. C., & Dabbs, J. M. (1998). The Hess pupil dilation findings: Sex or novelty? *Social Behavior and Personality: An International Journal*, *26*(4), 415-419.

Allman, J. M., Hakeem, A., Erwin, J. M., Nimchinsky, E., & Hof, P. (2001). The anterior cingulate cortex. *Annals of the New York Academy of Sciences*, *935*(1), 107-117.

American Psychiatric Associaiton. (2000). *Diagnostic and statistical manual of mental disorders* (4th ed., text rev.). Washington, DC: Author.

American Psychiatric Association. (2013). *Diagnostic and statistical manual of mental disorders* (5th ed.). Arlington, VA: American Psychiatric Publishing.

Aston-Jones, G., & Cohen, J. D. (2005). An integrative theory of locus coeruleus-norepinephrine function: adaptive gain and optimal performance. *Annual Review of Neuroscience*, *28*, 403-450.

Aston-Jones, G., Rajkowski, J., Kubiak, P., & Alexinsky, T. (1994). Locus coeruleus neurons in monkey are selectively activated by attended cues in a vigilance task. *Journal of Neuroscience*, *14*(7), 4467-4480.

Baker, S. L., Heinrichs, N., Kim, H. J., & Hofmann, S. G. (2002). The Liebowitz social anxiety scale as a self-report instrument: a preliminary psychometric analysis. *Behaviour research and therapy*, *40*(6), 701-715.

Bakes, A., Bradshaw, C. M., & Szabadi, E. (1990). Attenuation of the pupillary light reflex in anxious patients. *British journal of clinical pharmacology*, *30*(3), 377-381.

Bar-Haim, Y., Lamy, D., Pergamin, L., Bakermans-Kranenburg, M.J., van IJzendoorn, M.H. (2007). Threat-related attentional bias in anxious and nonanxious individuals: A meta-analytic study. *Psychological Bulletin, 133* (1), 1-24.

Barlow, D.H. (2002). “True alarms, false alarms, and learned anxiety”. In *Anxiety and its disorders: The nature and treatment of anxiety and panic*, 2nd edn, Edited by: Barlow, D.H. 219–251. New York: Guilford Press.

Beatty, J. (1982). Task-Evoked Pupillary Responses, Processing Load, and the Structure of Processing Resources, *Psychological Bulletin, 91* (2), 276-292.

Bebko, G. M., Franconeri, S. L., Ochsner, K. N., & Chiao, J. Y. (2011). Look before you regulate: differential perceptual strategies underlying expressive suppression and cognitive reappraisal. *Emotion*, *11*(4), 732.

Beidel, D. C., Turner, S. M., & Dancu, C. V. (1985). Physiological, cognitive and behavioral aspects of social anxiety. *Behaviour Research and Therapy*, *23*(2), 109-117.

Berridge, C. W., & Waterhouse, B. D. (2003). The locus coeruleus–noradrenergic system: modulation of behavioral state and state-dependent cognitive processes. *Brain Research Reviews*, *42*(1), 33-84.

Bijleveld, E., Custers, R., Aarts, H. (2009). The unconscious eye opener: Pupil dilation reveals strategic recruitment of resources upon presentation of subliminal reward cues. *Psychological Science*, *20*(11), 1313-1315.

Boev, A. N., Fountas, K. N., Karampelas, I., Boev, C., Machinis, T. G., Feltes, C., ... & Troup, C. (2005). Quantitative pupillometry: normative data in healthy pediatric volunteers. *Journal of Neurosurgery: Pediatrics*, *103*(6), 496-500.

Book, G., Stevens, M. C., Pearlson, G., & Kiehl, K. A. (2008). Fusion of fMRI and the pupil response during an auditory oddball task. In *Conference of the Cognitive Neuroscience Society*.

Bradley, M. M., Miccoli, L., Escrig, M. A., & Lang, P. J. (2008). The pupil as a measure of emotional arousal and autonomic activation. *Psychophysiology*, *45*(4), 602-607.

Browning, M., Behrens, T. E., Jocham, G., O'reilly, J. X., & Bishop, S. J. (2015). Anxious individuals have difficulty learning the causal statistics of aversive environments. *Nature Neuroscience*, *18*(4), 590.

Bruhl, A.B., Delsignore, A., Komossa, K., Weidt, S. (2014). Neuroimaging in social anxiety disorder- A meta-analytic review resulting in a new neurofunctional model. *Neuroscience and Behavioral Reviews, 47*, 260-280.

Burkhouse, K. L., Siegle, G. J., & Gibb, B. E. (2014). Pupillary reactivity to emotional stimuli in children of depressed and anxious mothers. *Journal of Child Psychology and Psychiatry*, *55*(9), 1009-1016.

Burkhouse, K. L., Siegle, G. J., Woody, M. L., Kudinova, A. Y., & Gibb, B. E. (2015). Pupillary reactivity to sad stimuli as a biomarker of depression risk: Evidence from a prospective study of children. *Journal of Abnormal Psychology*, *124*(3), 498.

Carter, M. E., Yizhar, O., Chikahisa, S., Nguyen, H., Adamantidis, A., Nishino, S., ... & De Lecea, L. (2010). Tuning arousal with optogenetic modulation of locus coeruleus neurons. *Nature Neuroscience*, *13*(12), 1526.

Cavanna, A. E., & Trimble, M. R. (2006). The precuneus: a review of its functional anatomy and behavioural correlates. *Brain*, *129*(3), 564-583.

Clark, D. (2001) A cognitive perspective on social phobia. *International Handbook of Social Anxiety: Concepts, Research and Interventions Relating to the Self and Shyness.* 405-430.

Clark, D. M., & McManus, F. (2002). Information processing in social phobia. *Biological Psychiatry*, *51*(1), 92-100.

Cohen, J. (1988). *Statistical power analysis for the behavioral sciences (2. Auflage)*. Hillsdale, NJ: Erlbaum.

Critchley, H., Tang, D., Glaser, D., Butterworth, B., Dolan, R.J. (2005) Anterior cingulate activity during error and autonomic response, *NeuroImage, 27,* 885-895.

Ebitz, R. B., & Moore, T. (2018). Both a gauge and a filter: Cognitive modulations of pupil size. *Frontiers in neurology*, *9*.

Eckman, P. S., & Shean, G. D. (1997). Habituation of cognitive and physiological arousal and social anxiety. *Behaviour Research and Therapy*, *35*(12), 1113-1121.

Erdfelder, E., Faul, F., & Buchner, A. (1996). GPOWER: A general power analysis program. *Behavior Research Methods, Instruments, & Computers*, *28*(1), 1-11.

Eysenck, M. (2014). *Anxiety and cognition: A unified theory*. Psychology Press.

Fox, E., Lester, V., Russo, R., Bowles, R. J., Pichler, A., & Dutton, K. (2000). Facial expressions of emotion: Are angry faces detected more efficiently? *Cognition & emotion*, *14*(1), 61-92.

Furmark, T. (2002). Social phobia: overview of community surveys. *Acta Psychiatrica Scandinavica*, *105*(2), 84-93.

Gerlach, A. L., Mourlane, D., & Rist, F. (2004). Public and private heart rate feedback in social phobia: A manipulation of anxiety visibility. *Cognitive Behaviour Therapy*, *33*(1), 36-45.

Gilzenrat, M. S., Cohen, J. D., Rajkowski, J., & Aston-Jones, G. (2003, November). Pupil dynamics predict changes in task engagement mediated by locus coeruleus. In *Society for Neuroscience Abstracts* (Vol. 515, p. 19).

Goldinger, S. D., & Papesh, M. H. (2012). Pupil dilation reflects the creation and retrieval of memories. *Current Directions in Psychological Science*, *21*(2), 90-95.

Granholm, E., Asarnow, R. F., Sarkin, A. J., & Dykes, K. L. (1996). Pupillary responses index cognitive resource limitations. *Psychophysiology, 33*(4), 457-461.

Granholm, E., Fish, S. C., & Verney, S. P. (2009). Pupillometric measures of attentional allocation to target and mask processing on the backward masking task in schizophrenia. *Psychophysiology*, *46*(3), 510-520.

Granholm, E., Morris, S., Asarnow, R. F., Chock, D., & Jeste, D. V. (2000). Accelerated age-related decline in processing resources in schizophrenia: evidence from pupillary responses recorded during the span of apprehension task. *Journal of the International Neuropsychological Society*, *6*(1), 30-43.

Granholm, E., Morris, S. K., Sarkin, A. J., Asarnow, R. F., & Jeste, D. V. (1997). Pupillary responses index overload of working memory resources in schizophrenia. *Journal of Abnormal Psychology*, *106*(3), 458.

Granholm, E., & Verney, S. P. (2004). Pupillary responses and attentional allocation problems on the backward masking task in schizophrenia. *International Journal of Psychophysiology*, *52*(1), 37-51.

Granholm, E., Verney, S. P., Perivoliotis, D., & Miura, T. (2006). Effortful cognitive resource allocation and negative symptom severity in chronic schizophrenia. *Schizophrenia Bulletin*, *33*(3), 831-842.

Heimberg, R. G., Brozovich, F. A., & Rapee, R. M. (2010). A cognitive behavioral model of social anxiety disorder: Update and extension. In *Social Anxiety (Second Edition)* (pp. 395-422).

Hepsomali, P., Hadwin, J.A., Liversedge, S.P., Garner, M. (2017). Pupillometric and saccadic measures of affective and executive processing in anxiety. *Biological Psychology, 127,* 173-179.

Hickey, L., Li, Y., Fyson, S. J., Watson, T. C., Perrins, R., Hewinson, J., ... & Pickering, A. E. (2014). Optoactivation of locus coeruleus neurons evokes bidirectional changes in thermal nociception in rats. *Journal of Neuroscience*, *34*(12), 4148-4160.

Hofmann, S. G. (2007). Cognitive factors that maintain social anxiety disorder: A comprehensive model and its treatment implications. *Cognitive Behaviour Therapy*, *36*(4), 193-209.

Hofmann, S. G., Newman, M. G., Ehlers, A., & Roth, W. T. (1995). Psychophysiological differences between subgroups of social phobia. *Journal of Abnormal Psychology*, *104*(1), 224.

Honma, M., Tanaka, Y., Osada, Y., & Kuriyama, K. (2012). Perceptual and not physical eye contact elicits pupillary dilation. *Biological Psychology*, *89*(1), 112-116.

Hughes, M. S. (1991). Dictionary of eye terminology. *Archives of Ophthalmology*, *109*(9), 1208-1208.

Joshi, S., Li, Y., Kalwani, R. M., & Gold, J. I. (2016). Relationships between pupil diameter and neuronal activity in the locus coeruleus, colliculi, and cingulate cortex. *Neuron*, *89*(1), 221-234.

Kahneman, D., & Beatty, J. (1966). Pupil diameter and load on memory. *Science*, *154*(3756), 1583-1585.

Kaufman, P. L., Levin, L. A., Adler, F. H., & Alm, A. (2011). *Adler's Physiology of the Eye*. Elsevier Health Sciences.

Keil, V., Hepach, R., Vierrath, S., Caffier, D., Tuschen-Caffier, B., Klein, C., & Schmitz, J. (2018). Children with social anxiety disorder show blunted pupillary reactivity and altered eye contact processing in response to emotional faces: Insights from pupillometry and eye movements. *Journal of anxiety disorders*, *58*, 61-69.

Kessler, R. C., Berglund, P., Demler, O., Jin, R., Merikangas, K. R., & Walters, E. E. (2005). Lifetime prevalence and age-of-onset distributions of DSM-IV disorders in the National Comorbidity Survey Replication. *Archives of General Psychiatry*, *62*(6), 593-602.

Kimble, M. O., Fleming, K., Bandy, C., Kim, J., & Zambetti, A. (2010). Eye tracking and visual attention to threating stimuli in veterans of the Iraq war. *Journal of Anxiety Disorders*, *24*(3), 293-299.

Kohnen, E. M., Zubcov, A. A., & Kohnen, T. (2004). Scotopic pupil size in a normal pediatric population using infrared pupillometry. *Graefe's Archive for Clinical and Experimental Ophthalmology*, *242*(1), 18-23.

Koikegami, H., & Yoshida, K. (1953). Pupillary dilatation induced by stimulation of amygdaloid nuclei. *Psychiatry and Clinical Neurosciences*, *7*(2), 109-126.

Koster, E. H., Crombez, G., Verschuere, B., & De Houwer, J. (2006). Attention to threat in anxiety-prone individuals: Mechanisms underlying attentional bias. *Cognitive Therapy and Research*, *30*(5), 635-643.

Kret, M., Stekelenburg, J., Roelofs, K., & De Gelder, B. (2013). Perception of face and body expressions using electromyography, pupillometry and gaze measures. *Frontiers in Psychology*, *4*, 28.

Kudinova, A. Y., Burkhouse, K. L., Siegle, G., Owens, M., Woody, M. L., & Gibb, B. E. (2016). Pupillary reactivity to negative stimuli prospectively predicts recurrence of major depressive disorder in women. *Psychophysiology*, *53*(12), 1836-1842.

MacLachlan, C., & Howland, H. C. (2002). Normal values and standard deviations for pupil diameter and interpupillary distance in subjects aged 1 month to 19 years. *Ophthalmic and Physiological Optics*, *22*(3), 175-182.

Maratos, F. A. (2011). Temporal processing of emotional stimuli: The capture and release of attention by angry faces. *Emotion*, *11*(5), 1242.

Mars, R. B., & Grol, M. J. (2007). Dorsolateral prefrontal cortex, working memory, and prospective coding for action. *Journal of Neuroscience*, *27*(8), 1801-1802.

Mathews, A., Mackintosh, B., & Fulcher, E. P. (1997). Cognitive biases in anxiety and attention to threat. *Trends in cognitive sciences*, *1*(9), 340-345.

McCall, J. G., Al-Hasani, R., Siuda, E. R., Hong, D. Y., Norris, A. J., Ford, C. P., & Bruchas, M. R. (2015). CRH engagement of the locus coeruleus noradrenergic system mediates stress-induced anxiety. *Neuron*, *87*(3), 605-620.

McQuaid, J. R., Stein, M. B., Laffaye, C., & McCahill, M. E. (1999). Depression in a primary care clinic: the prevalence and impact of an unrecognized disorder. *Journal of Affective Disorders*, *55*(1), 1-10.

Minassian, A., Granholm, E., Verney, S., & Perry, W. (2004). Pupillary dilation to simple vs. complex tasks and its relationship to thought disturbance in schizophrenia patients. *International Journal of Psychophysiology*, *52*(1), 53-62.

Mogg, K., & Bradley, B. P. (1998). A cognitive-motivational analysis of anxiety. *Behaviour research and therapy*, *36*(9), 809-848.

Mogg, K., & Bradley, B. P. (2002). Selective orienting of attention to masked threat faces in social anxiety. *Behaviour research and therapy*, *40*(12), 1403-1414.

Mogg, K., Philippot, P., & Bradley, B. P. (2004). Selective attention to angry faces in clinical social phobia. *Journal of abnormal psychology*, *113*(1), 160.

Moscovitch, D. A. (2009). What is the core fear in social phobia? A new model to facilitate individualized case conceptualization and treatment. *Cognitive and Behavioral Practice*, *16*(2), 123-134.

Müller-Pinzler, L., Gazzola, V., Keysers, C., Sommer, J., Jansen, A., Frässle, S., ... & Krach, S. (2015). Neural pathways of embarrassment and their modulation by social anxiety. *NeuroImage*, *119*, 252-261.

Nassar, M. R., Rumsey, K. M., Wilson, R. C., Parikh, K., Heasly, B., & Gold, J. I. (2012). Rational regulation of learning dynamics by pupil-linked arousal systems. *Nature Neuroscience*, *15*(7), 1040.

Oakman, J., Van Ameringen, M., Mancini, C., & Farvolden, P. (2003). A confirmatory factor analysis of a self-report version of the Liebowitz Social Anxiety Scale. *Journal of Clinical Psychology*, *59*(1), 149-161.

Öhman, A. (1996). Preferential preattentive processing of threat in anxiety: Preparedness and attentional biases. *Current controversies in the anxiety disorders*, *2*, 253-290.

Pannekoek, J. N., Veer, I. M., van Tol, M. J., van der Werff, S. J., Demenescu, L. R., Aleman, A., ... & van der Wee, N. J. (2013). Resting-state functional connectivity abnormalities in limbic and salience networks in social anxiety disorder without comorbidity. *European Neuropsychopharmacology*, *23*(3), 186-195.

Partala, T., & Surakka, V. (2003). Pupil size variation as an indication of affective processing. *International Journal of Human-Computer Studies*, *59*(1-2), 185-198.

Patwari, P. P., Stewart, T. M., Rand, C. M., Carroll, M. S., Kuntz, N. L., Kenny, A. S., ... & Weese-Mayer, D. E. (2012). Pupillometry in congenital central hypoventilation syndrome (CCHS): quantitative evidence of autonomic nervous system dysregulation. *Pediatric Research*, *71*(3), 280.

Peavler, W. S. (1974). Pupil size, information overload, and performance differences. *Psychophysiology*, *11*(5), 559-566.

Price, M., Tone, E. B., & Anderson, P. L. (2011). Vigilant and avoidant attention biases as predictors of response to cognitive behavioral therapy for social phobia. *Depression and Anxiety*, *28*(4), 349-353.

Price, R. B., Siegle, G. J., Silk, J. S., Ladouceur, C., McFarland, A., Dahl, R. E., & Ryan, N. D. (2013). Sustained neural alterations in anxious youth performing an attentional bias task: A pupilometry study. *Depression and Anxiety*, *30*(1), 22-30.

Proulx, T., Sleegers, W., & Tritt, S. M. (2017). The expectancy bias: Expectancy-violating faces evoke earlier pupillary dilation than neutral or negative faces. *Journal of Experimental Social Psychology*, *70*, 69-79.

Purves, D., Augustine, G. J., Fitzpatrick, D., Hall, W. C., LaMantia, A. S., McNamara, J. O., & White, L. E. (2008). Neuroscience, Fourth Ed.

Rapee, R. M., & Heimberg, R. G. (1997). A cognitive-behavioral model of anxiety in social phobia. *Behaviour Research and Therapy*, *35*(8), 741-756.

Reimer, J., McGinley, M. J., Liu, Y., Rodenkirch, C., Wang, Q., McCormick, D. A., & Tolias, A. S. (2016). Pupil fluctuations track rapid changes in adrenergic and cholinergic activity in cortex. *Nature Communications*, *7*, 13289.

Reiss, S. (1991). Expectancy model of fear, anxiety, and panic. *Clinical Psychology Review*, *11*(2), 141-153.

Rosen, D. (2017) *Attention during virtual peer feedback in youth with a history of anxiety compared to healthy youth.* Unpublished master's thesis, University of Pittsburgh, Pittsburgh, Pennsylvania.

Schmitz, J., Krämer, M., Tuschen-Caffier, B., Heinrichs, N., & Blechert, J. (2011). Restricted autonomic flexibility in children with social phobia. *Journal of Child Psychology and Psychiatry*, *52*(11), 1203-1211.

Schmitz, J., Tuschen-Caffier, B., Wilhelm, F. H., & Blechert, J. (2013). Taking a closer look: autonomic dysregulation in socially anxious children. *European child & adolescent psychiatry*, *22*(10), 631-640.

Shechner, T., Jarcho, J. M., Britton, J. C., Leibenluft, E., Pine, D. S., & Nelson, E. E. (2013). Attention bias of anxious youth during extended exposure of emotional face pairs: An eye-tracking study. *Depression and Anxiety*, *30*(1), 14-21.

Siegle, G. J., Granholm, E., Ingram, R. E., & Matt, G. E. (2001). Pupillary and reaction time measures of sustained processing of negative information in depression. *Biological Psychiatry*, *49*(7), 624-636.

Siegle, G. J., Steinhauer, S. R., & Thase, M. E. (2004). Pupillary assessment and computational modeling of the Stroop task in depression. *International Journal of Psychophysiology*, *52*(1), 63-76.

Siegle, G. J., Steinhauer, S. R., Carter, C. S., Ramel, W., & Thase, M. E. (2003). Do the seconds turn into hours? Relationships between sustained pupil dilation in response to emotional information and self-reported rumination. *Cognitive Therapy and Research, 27*(3), 365-382.

Siegle, G. J., Steinhauer, S. R., Stenger, V. A., Konecky, R., & Carter, C. S. (2003). Use of concurrent pupil dilation assessment to inform interpretation and analysis of fMRI data. *Neuroimage*, *20*(1), 114-124.

Silk, J. S., Dahl, R. E., Ryan, N. D., Forbes, E. E., Axelson, D. A., Birmaher, B., & Siegle, G. J. (2007). Pupillary reactivity to emotional information in child and adolescent depression: links to clinical and ecological measures. *American Journal of Psychiatry*, *164*(12), 1873-1880.

Silk, J. S., Stroud, L. R., Siegle, G. J., Dahl, R. E., Lee, K. H., & Nelson, E. E. (2011). Peer acceptance and rejection through the eyes of youth: pupillary, eyetracking and ecological data from the Chatroom Interact task. *Social Cognitive and Affective Neuroscience*, *7*(1), 93-105.

Silk, J. S., Siegle, G. J., Whalen, D. J., Ostapenko, L. J., Ladouceur, C. D., & Dahl, R. E. (2009). Pubertal changes in emotional information processing: Pupillary, behavioral, and subjective evidence during emotional word identification. *Development and Psychopathology*, *21*(1), 7-26.

Simpson, H. M., & Molloy, F. M. (1971). Effects of audience anxiety on pupil size. *Psychophysiology*, *8*; 491-496.

Snyder, K., Wang, W. W., Han, R., McFadden, K., & Valentino, R. J. (2012). Corticotropin-releasing factor in the norepinephrine nucleus, locus coeruleus, facilitates behavioral flexibility. *Neuropsychopharmacology*, *37*(2), 520.

Staugaard, S. R., & Rosenberg, N. K. (2011). Processing of emotional faces in social phobia. *Mental illness*, *3*(1).

Steinhauer, S. R. (1983). Pupillary dilation to emotional visual stimuli revisited. *Psychophysiology*, *20*, S472.

Steinhauer, S. R., & Hakerem, G. (1992). The pupillary response in cognitive psychophysiology and schizophrenia. *Annals of the New York Academy of Sciences*, *658*(1), 182-204.

Steinhauer, S. R., Siegle, G. J., Condray, R., & Pless, M. (2004). Sympathetic and parasympathetic innervation of pupillary dilation during sustained processing. *International Journal of Psychophysiology*, *52*(1), 77-86.

Steinhauer, S., & Zubin, J. (1982). Vulnerability to schizophrenia: Information processing in the pupil and event-related potential. In *Biological Markers in Psychiatry and Neurology* (pp. 371-385).

Stopa, L., & Clark, D. M. (2000). Social phobia and interpretation of social events. *Behaviour Research and Therapy*, *38*(3), 273-283.

Szabadi, E. (2012). Modulation of physiological reflexes by pain: role of the locus coeruleus. *Frontiers in Integrative Neuroscience*, *6*, 94.

Tottenham, N., Tanaka, J. W., Leon, A. C., McCarry, T., Nurse, M., Hare, T. A., ... & Nelson, C. (2009). The NimStim set of facial expressions: judgments from untrained research participants. *Psychiatry Research*, *168*(3), 242-249.

Valentino, R. J., & Van Bockstaele, E. (2008). Convergent regulation of locus coeruleus activity as an adaptive response to stress. *European Journal of Pharmacology, 583*(2-3), 194-203.

Vazey, E. M., & Aston-Jones, G. (2014). Designer receptor manipulations reveal a role of the locus coeruleus noradrenergic system in isoflurane general anesthesia. *Proceedings of the National Academy of Sciences, 111*(10), 3859-3864.

Walker, E., & Harvey, P. (1986). Positive and negative symptoms in schizophrenia: attentional performance correlates. *Psychopathology, 19*(6), 294-302.

Wang, J. T. Y. (2011). Pupil dilation and eye tracking. *A handbook of process tracing methods for decision research: A critical review and user's guide*, 185-204.

Waters, A. M., Mogg, K., & Bradley, B. P. (2012). Direction of threat attention bias predicts treatment outcome in anxious children receiving cognitive-behavioural therapy. *Behaviour Research and Therapy*, *50*(6), 428-434.

White, T. L., & Depue, R. A. (1999). Differential association of traits of fear and anxiety with norepinephrine-and dark-induced pupil reactivity. *Journal of Personality and Social Psychology*, *77*(4), 863.

Williams, J. M. G., Watts, F. N., MacLeod, C., & Mathews, A. (1988). Cognitive psychology and emotional disorders. Chichester: Wiley.

Wilson, M., Smith, N. C., Chattington, M., Ford, M., & Marple-Horvat, D. E. (2006). The role of effort in moderating the anxiety–performance relationship: Testing the prediction of processing efficiency theory in simulated rally driving. *Journal of Sports Sciences, 24*(11), 1223-1233.

Yoon, K. L., & Zinbarg, R. E. (2008). Interpreting neutral faces as threatening is a default mode for socially anxious individuals. *Journal of Abnormal Psychology, 117*(3), 680.

Zald, D. H. (2003). The human amygdala and the emotional evaluation of sensory stimuli. *Brain Research Reviews*, *41*(1), 88-123.