Pupillary assessment and computational modeling of the Stroop task in depression

Greg J. Siegle*, Stuart R. Steinhauer, Michael E. Thase

Western Psychiatric Institute and Clinic, University of Pittsburgh, 3811 O’Hara St., Pittsburgh, PA 15213, USA
VA Pittsburgh Healthcare System, Pittsburgh, PA, USA

Abstract

Depressed individuals frequently display disruptions in selective attention, but the time course and specificity of these difficulties are not well-understood. To better understand the nature of attentional disruptions in depression, 28 healthy adults and 23 unmedicated depressed adults completed a Stroop color-naming task using a long inter-stimulus interval and pupil dilation was recorded as a measure of cognitive load. Both groups took longer to name the color for incongruent than congruent trials. Pupil dilation was also larger for incongruent trials than for congruent trials across groups, which suggested that pupil dilation reflected cognitive load on the task. Though the groups did not differ in the magnitude of Stroop effect in pupil dilation, depressed individuals displayed decreased pupil dilation in the seconds following stimuli relative to controls. Computational neural network modeling further suggested that observed effects were consistent with decreased prefrontal cortex activity, associated with decreased cognitive control.

Keywords: Depression; Neural network; Stroop; Interference; Pupil dilation; Attention

1. Introduction

There is largely a consensus that selective attention is impaired in depressed individuals (e.g. Ottowitz et al., 2002). Yet, the nature of that impairment is open to some debate due to variability in results on behavioral and neuropsychological tasks used to measure selective attention in depressed individuals. This manuscript highlights potential underlying explanations for this observed variability as a function of differential disruptions over the time-course of processing on selective attention tasks in depressed individuals. Healthy never-depressed individuals and unmedicated depressed individuals completed a widely used measure selective-attention, the Stroop Color Naming Task, during measurement of pupil dilation, which allowed examination of the time-course of attentional allocation during each trial on the task. We use a popular computational neural-network model of the Stroop task to explore potential mechanisms underlying differences in pupil dilation in depressed and never-depressed individuals on the task.

The Stroop Color Naming task is one of the best-studied measures of selective attention. In this task, individuals are required to name the color ink in which words that are the names of colors are written. In general people react slower, and
make more errors when the presented word is incongruent with the color in which it is written (e.g. the word ‘red’ written in blue) than when the color and word are congruent (see Macleod, 1992, for a review). The task is generally thought to measure the degree to which individuals are able to inhibit a pre-potent response (word-reading) in the face of a task that takes attentional control. A host of neuroimaging studies suggest that the task is associated with activity in a number of brain areas, particularly prefrontal cortex, and that a number of brain areas are more strongly activated during incongruent than congruent stimuli, most notably the anterior cingulate cortex and frontal pole (MacDonald et al., 2000).

Though a number of studies have examined performance by depressed individuals on the Stroop task, and all have found some impairment (see Ottowitz et al., 2002 for a review), the types of detected impairment vary. For example, depressed individuals have been observed to display more errors on incongruent stimuli (Lockwood et al., 2002; Schatzberg et al., 2000). Other studies do not find differences in error rates but do find that in general, depressed individuals react slower than never-depressed individuals on the task (Degl’Innocenti et al., 1998). Some studies do not demonstrate particularly slowed reactions to incongruent stimuli in depressed individuals relative to controls (Degl’Innocenti et al., 1998) though others do (Lemelin et al., 1997). There are many differences in the way the task is administered between studies including the rate at which stimuli are presented, whether stimuli are blocked, and whether multiple stimuli were visible at one time suggesting potentially, that if there are different disruptions throughout the time-course of processing Stroop stimuli in depressed individuals, these could lead to variability in behavioral results.

Thus, to better understand the time-course of information-processing on the Stroop task, we administered a single-word presentation version of the task to depressed and never depressed individuals during measurement of pupil dilation in which there was adequate time between stimuli to assess the entire time-course of information processing. Many studies have demonstrated pupil dilation to be a reliable correlate of cognitive load, as the pupil dilates more under conditions of higher attentional allocation, memory use, or interpretation of more difficult material (see Beatty, 1982a or Steinhaeuer and Hakerem, 1992, for reviews). Pupil dilation persists if the demand is sustained (e.g. Beatty, 1982b). For example, as individuals are asked to remember larger number of digits, for example, pupil dilation increases proportionally (e.g. Kahneman and Beatty, 1966; Granholm et al., 1996). Thus, the pupil has been shown to reflect the time course of activity in brain areas associated with cognitive processing such as the dorso-lateral prefrontal cortex (Siegle et al., 2003b). The pupil has also been shown to dilate in response to emotional information (e.g. Janisse, 1973) and is innervated by brain areas associated with both cognitive and emotional processing (e.g. Szabadi and Bradshaw, 1996).

Of particular note, we have previously shown that pupil dilation increases to incongruent words relative to congruent words on the Stroop task (Brown et al., 1999). We have also demonstrated disruptions in the time-course of information processing in depressed individuals, showing that depressed individuals tend to display sustained pupil dilation in response to tasks requiring participants to attend to the emotional content of words (Siegle et al., 2001, 2003a).

We expected that if depressed individuals displayed increased Stroop interference, they would display greater peak pupil dilation to incongruent stimuli than healthy individuals. It was unclear whether they would also display differences during preparation for stimuli or sustained pupil dilation in response to incongruent stimuli. Decreased preparatory pupil dilation could indicate a failure to recruit relevant attentional resources. Increased sustained dilation could indicate a failure to disengage from stimuli. In contrast, decreased sustained dilation could indicate a lack of investment in the task, or quick redirection of attentional resources away from this non-emotional task to something else, potentially a pre-task contemplation of emotional information.

Thus, our primary questions were the following: (1) Could we detect Stroop interference with pupil dilation (as a check on the method)? (2) Did depressed individuals display different patterns of
pupil dilation from healthy individuals? (3) Did disruptions in pupil dilation to one trial persist into the next trial? and (4) What cognitive and brain mechanisms could give rise to observed group differences in pupil dilation? The results section is structured to answer the first three questions. Computational network modeling is used to generate speculation regarding the fourth question.

2. Method

2.1. Participants

Participants included 23 patients (12 Male, 18 Caucasian, three African American, two biracial, ages 19–55, M(S.D.)_age = 40.3 (12.09), M(S.D.)_education = 15.4(2.2)) diagnosed with unipolar major depression using a structured clinical interview (SCID I; First et al., 1996) and 28 healthy, never depressed controls (10 Male, 24 Caucasian, 1 African American, 1 Asian, 2 biracial, ages 21–50, M(S.D.)_age = 31.1(8.8), M(S.D.)_education = 16.7(1.4)). Depressed participants had moderate depressive severity, M(SD) BDI = 25.4(11.3), and reported previously having had from one to more than 10 previous episodes of depression, Median (Md) = 10 episodes. Control participants had mild depressive severity, M(S.D) BDI = 3.5(4.2) and had no current or historical Axis I disorder using the SCID interview. Participants stated that they had no significant eye problems; a subset who were assessed with a handheld eye chart had normal corrected vision (20/30) with both eyes open; the remainder reported no difficulty reading text on a computer screen much smaller than the text used in the experiment. Participants described no health problems thought to interfere with performance or psychoactive drug abuse within the past six months. No depressed participants were taking, or had taken antidepressants within two-weeks of testing, or prozac within six-weeks of testing. Participants were excluded if they had a previous history of psychosis, or manic episodes. Fifty-one participants reported no alcohol abuse in the past six months; one participant’s data was ambiguous in this regard, and the participant could not be recontacted. All participants scored in the normal range on a cognitive screen (NAART-II VIQ > 80; Nelson and Willison, 1991). Control participants were significantly younger, t(39.3) = 3.0, P = 0.004, and better educated, t(35.8) = 2.4, P = 0.02, but did not differ significantly in gender or ethnic composition.

2.2. Apparatus

Stimuli were displayed in black on a white computer screen. Participants sat approximately 65.5 cm from the bottom of the stimulus. Stimuli were lowercase letters approximately 1.59 cm high, subtending 1.4° of visual angle. Reaction times were recorded using a game pad capable of reading reaction times with millisecond resolution. It was modified to contain three buttons, arranged in a triangle, so that respondents’ fingers were nearly equidistant from each possible response. To account for differential response latencies to different buttons, the mapping of game-pad buttons to responses was counterbalanced across participants.

Pupil dilation was recorded using methods previously described and tested (e.g. Steinhauer et al., 2000) at the VA Pittsburgh Healthcare System. In brief, data were collected using an ISCAN RK406 pupillometer. The pupillometer consisted of a video camera and infrared light source that were pointed at a participant’s eye, and a device that tracked the location and size of the pupil using these tools. Pupil size was recorded at 62.5 Hz (every 16 ms) and passed digitally from the pupillometer to a computer that stored the acquired data along with signals marking the beginning of trials, the end of fixation, stimulus onset time, and reaction time. The pupillometer’s resolution for a typical participant was better than 0.025-mm pupil diameter. Data collection was managed using EEG-SYS (Hartwell, 1995).

2.3. Procedure

At a first appointment, participants were told about the experiment, and signed University of Pittsburgh and VA Pittsburgh IRB approved consent forms. Participants received a brief vision test and the NAART. At a second appointment, within two weeks, participants completed a battery of
information processing measures, including the Stroop task. Testing occurred in a moderately lit room (0.56 foot-candles illuminance) in which the experimenter was not present. Time of day was not controlled for. The order of the tasks was counterbalanced across participants.

2.4. Tasks

The Stroop task was chosen because there is a wealth of behavioral and psychophysiological data on it, because it takes a few seconds to complete a trial, and is easy enough that depressed individuals would not get frustrated by the task. Participants viewed a fixation mask (row of X’s with vertical prongs over the center) for 1 s followed by a color-word for 150 ms, followed by a mask (row of X’s) for 8 s. Trials were consistently paced. Participants were instructed to push a button for the color in which the word was written (red, green or blue). The order of these buttons was counterbalanced across participants and the first letter of each color name was always displayed in the upper right corner of the screen to cue subjects to the button order.

2.5. Measures of mood

To assess depressive severity at the time of testing, the Beck Depression Inventory II (BDI; Beck et al., 1996) was administered. The BDI has repeatedly been validated as a measure of depressive severity in control and adult depressed populations.

2.6. Data selection, cleaning and reduction

2.6.1. Selection of stimuli for analysis

Trials with reaction times below 150 ms were discarded as outliers, because previous results suggest that reaction times in this range indicate that a response was made without regard for the stimulus (Matthews and Southall, 1991). Incorrect trials were also eliminated from pupil dilation averages.

2.6.2. Calculation of pupil dilation indices

Data were cleaned using methodology previously described by Granholm (e.g. Granholm et al., 1996). Blinks were identified as large changes in pupil dilation occurring too rapidly to signify actual dilation or contraction. Trials comprised of over 50% blinks were removed from consideration. Linear interpolations replaced blinks throughout the data set. Data were smoothed using a ten point weighted average filter. Then, linear trends in pupil dilation calculated over blocks of 20 trials were removed from pupil dilation data to eliminate effects of slow drift in pupil diameter that were not related to trial characteristics. Pupil diameter, measured as the average dilation over the 1 s preceding the onset of the stimulus, was subtracted from pupil diameter after stimulus onset to produce pupil dilation difference score indices. Stimulus selection and data cleaning procedures resulted in the elimination of Md = 3, M(S.D.) = 5.8 (7.2) trials per subject.

2.6.3. Analytic strategy

Within and between-group contrasts on pupil dilation were examined via statistical tests at each point along pupil dilation waveforms, downsampled to 10 Hz. As pupil dilation waveforms are highly autocorrelated ($r_{xx}>0.9$) these tests could not be considered independent; rather, Guthrie and Buchwald’s (1991) technique was used to define a region over which a series of contiguous point-by-point tests could be considered significant; using this entire technique. Seven second windows of consecutive tests, significant at $P<0.1$ were interpreted as statistically significant. This strategy uses consecutive points on a waveform as replications to control for type 1 error at $P=0.05$ for all tests along a given waveform. Autocorrelation is accounted for via Monte Carlo simulations of the maximum length of adjacent significant tests present in simulated data with a similar autocorrelation structure to acquire empirical data. It has been used previously to understand event-related brain potential data (e.g. Guthrie and Buchwald, 1991) as well as pupil dilation data (Siegle et al., 2003a,b).

To implement Guthrie and Buchwald’s (1991) strategy, we defined two independent families of tests, one encompassing tests occurring in the first 6 s of the trial (preparation and peak processing) and another family of tests occurring in the last 6 s.
s of the trial, associated with sustained processing. Monte Carlo simulations were used to find the maximum sequence length that occurred less than 5% of the time in series with similar autocorrelation to the empirical data; simulated time-series with a given autocorrelation were constructed using Strauss’s algorithm (Strauss, 2000). To account for autocorrelation associated with relevant signals, which should not count against significant tests, the residual autocorrelation after removing variance attributable to the first few principal components was used, as per Guthrie and Buchwald’s recommendations. An estimate of four principal components was used in the first 6 s, and two principal components in the remaining time, based on inspection of scree plots. This principal components structure is similar to that found in other studies in which PCA was performed on pupil dilation (e.g. Siegle et al., 2001). The residual autocorrelation in each segment was thus estimated to be 88. The maximum sequence length in 100 runs of 100 simulations of 51 simulated subjects 120 points long (12 s at a.1 Hz sampling rate) was 7 points, which corresponded to 0.7 s.

Main effects of congruence (e.g. differential response to congruent vs. incongruent stimuli) were examined using paired t-tests. Main effects of group were evaluated using independent samples t-tests. Group by congruence interactions were evaluated using hierarchical regressions on responses to incongruent words in which responses to congruent stimuli were entered on the first step and incremental variance due to group was tested. This type of analysis is similar to a standard MANOVA contrast but does not rely on difference variances, which can be unreliable (e.g. Cohen and Cohen, 1983, p. 414).

3. Results

3.1. Behavioral data

Mean harmonic mean decision times were computed for each individual for each condition and are presented, along with error rates, in Table 1. Error and decision time data were subjected to two congruence (congruent, incongruent) × 2 group (depressed, control) split plot multivariate analysis of variance (MANOVA). As shown in Table 1, participants made very few errors on the task though the analysis revealed a main effect of condition: participants made more incongruent than congruent errors, \( F(1,49) = 10.4, P = 0.002 \), proportion of variance accounted for (\( \eta^2 \)) = 0.18. Patients were slightly but not significantly more accurate than control participants, \( F(1,49) = 2.96, P = 0.09, \eta^2 = 0.06 \). The interaction of group by condition was not significant, \( P > 0.05, \eta^2 < 0.01 \).

Similarly a group×condition MANOVA on decision times revealed a significant main effect of congruence; all individuals were slower to name the color of incongruent stimuli, \( F(1,49) = 113.04, P < 0.0001, \eta^2 = 0.70 \), Mean Difference (\( D \)) = 141 ms, M(S.D.)\text{congruent} = 840.26 (305.02) ms, M(S.D.)\text{incongruent} = 981.35 (331.03) ms. Depressed individuals tended to be slower to respond to all stimuli than control participants, \( F(1,49) = 3.13, P = 0.08, \eta^2 = 0.06, D = 153 \) ms. The group by condition interaction was not significant, \( P > 0.05, \eta^2 < 0.02 \). Regression analysis revealed that decision times to congruent stimuli accounted for 91% of the variation in reaction times to incongruent stimuli, leaving little room for additional variance to be accounted for by group. Mean reaction time variables were not significantly correlated with accuracy.

3.2. Does pupil dilation reflect stroop interference in the current experiment?

To examine the extent to which Stroop interference could be detected using pupil dilation, mean pupillary waveforms were computed for each participant, for each condition. As expected, peak
Fig. 1. Grand mean waveforms for the basic Stroop effect. Regions of statistically significant differences in paired t-tests are highlighted along the X-axis. Areas shaded darker are significant at $P<0.05$; areas shaded lighter are significant at $P<0.1$.

Pupil dilation was larger for incongruent than congruent trials, $t(50)=3.54$, $P=0.001$, $d=1.77$, $M$(S.D.)congruent=0.28(0.14) mm, $M$(S.D.)incongruent=0.33(0.16) mm.

To illustrate the extent to which time windows other than the peak differed, condition-related differences were evaluated at each sample along the grand-mean waveforms via paired-t-tests. The top panel of Fig. 1 shows the grand mean waveforms for each condition, across all participants. Significant differences are marked along the X-axis in Fig. 1; lightly shaded windows represent $P<0.1$ and darkly shaded windows represent $P<0.05$.

There was one significantly long window post-stimulus extending from 1.74 to 3.28 s after the beginning of a trial (stimulus onset occurred at 1 s), as determined using Guthrie and Buchwald (1991) method. The mean difference in the window (D) was 0.03 mm, $t(50)=3.22$, $P<0.0005$.

These data suggest that condition-related differences occurred primarily in the vicinity of the peak pupil dilation. To see whether these observations generalized to both groups, the mean pupil dilation waveforms were plotted separately for each group (Fig. 1—bottom panels). As shown in the figures, significant Stroop effects were present in each group's pupil dilation around the time of the peak (Controls: 1.94–2.80 s, $D=0.04$ mm; $t(27)=2.49$, $P=0.02$, Depressed: 1.55–3.95 s: $M=0.03$ mm, $t(22)=3.06$, $P=0.01$). Thus, pupil dilation appears to be an adequate measure of Stroop interference.

Another way to demonstrate that pupil dilation is reflective of behavioral performance is to show that reaction times are systematically related to some feature of the pupil dilation waveform.
Though the magnitude of interference in pupil dilation was not related to the magnitude of interference in reaction times on a between-subjects basis ($r = -0.1$), peak pupil dilation was significantly correlated with reaction times within subjects, mean correlation ($M_r = 0.23, t(50) = 6.8, P < 0.0005$). Examination of correlations of pupil dilation at each time point with reaction times revealed that pupil dilation 0.9 s following the stimulus was best correlated with reaction time, $M_r = 0.35$. Similarly, examining correlations between each sample along reaction-time-locked pupil dilation waveforms and reaction times revealed that pupil dilation 0.7 s preceding participants’ reaction times was best correlated with reaction times, $M_r = 0.59$.

3.3. Did depressed individuals display different patterns of pupil dilation than healthy control participants?

To examine group differences in peak dilation, a group\(\times\)condition ANOVA was performed on the peak amplitude of each participant’s mean pupillary waveform for each condition. This analysis revealed the larger peak dilation in the incongruent than congruent condition, described previously, $F(1,49) = 11.98, P = -0.001, \eta^2 = 0.20$, but no main effects or interactions with group. Moreover, no significant group\(\times\)condition interactions were detected at any point along the pupil-dilation waveforms.

Fig. 2 shows the group grand-mean waveforms, averaged over both conditions, along with significant differences in $t$-tests performed along these waveforms. As shown in the figure, pupillary responses for depressed individuals appeared delayed compared to control participants. Thus, depressed individuals revealed decreased pupil dilation during the preparatory and pre-peak period from 6 to 1.2 s. Mean Difference ($D$) = 0.03 mm, $t(49) = 2.08, P = 0.04$, Cohen’s $d = 0.59$; this region was not long enough to be considered statistically significant using Guthrie and Buchwald’s (1991) criteria. In addition, depressed individuals had decreased pupil dilation in the later portion of the trial, 6.35–8.75 s, $D = 0.05$ mm, $t(49) = 2.03, P = 0.05$, $d = 0.57$. Dilation in the early and late regions was weakly correlated between subjects, $r = 0.02$, though dilation in the early region was moderately related across trials within subjects, mean $r = 0.30$, suggesting that trials on which decreased dilation occurred many seconds after the response were the same trials on which there was little initial response, across subjects.

3.4. Was decreased sustained dilation related to processing on subsequent trials?

To suggest that decreased sustained dilation in depressed individuals could affect performance on selective attention tasks it is useful to show that sustained physiological activity on one trial affects physiological or behavioral performance on subsequent trials. In fact, mean pupil diameter in the late region, 6.35–8.75 s following a stimulus was moderately correlated with pupil diameter at the beginning of the following trial, mean $r = 0.43$, which was significant upon a one-sample $t$-test of the Fisher’s $z$-transformed correlations, $t(50) = 13.47, P < 0.0005$, and remained correlated with pupil diameter in the early window associated with group differences (0.6 to 1.2 s) on the next trial mean $r = 0.37, t(50) = 12.4, P < 0.0005$. Yet, there was little relationship between decreased sustained pupil dilation and reaction time on the subsequent trial ($r < 0.01$), potentially suggesting that subsequent behavioral correlates of sustained pupil dilation were too weak to be observed in the current design. As sustained dilation was also positively correlated with dilation in the peak window (1.74–
3.82 s) of the following trial which occurred approximately 7 s later, mean \( r = 0.25, t(50) = 8.7, P < 0.0005 \), the data suggest that higher pupil dilation in one trial would be associated with higher cognitive load in the relevant portion of subsequent trials. For comparison, the mean autocorrelation of pupillary data in this experiment at a similar lag of 7 s was 0.004, suggesting that the observed relationship was larger than would be expected by the signal’s autocorrelation.

3.5. Sensitivity analyses

3.5.1. Age effects
To examine the extent to which age mediated observed effects, the same analyses were run on a better age-matched subsample of 20 depressed and 20 control participants formed by eliminating the oldest three depressed participants and youngest 8 control participants, \( D = 3.6 \) years, \( t(38) = -1.1, P = 0.26 \). Significant effects of congruence on reaction time and pupil dilation near the peak remained and no group differences in these contrasts were apparent. Decreased sustained dilation was also preserved in the depressed group; depressed individuals displayed significantly decreased dilation from 6.1–8.8 s, \( D = 0.05 \) mm, \( t(38) = 1.94, P = 0.06, d = 0.61, \) and from 10.3–11.0 s, \( D = 0.02 \) mm, \( t(38) = 1.95, P = 0.06, d = 0.62 \) relative to control participants.

3.5.2. Effects of delayed reaction times
To examine the extent to which effects could have been due to variability in response latency (e.g. depressed individuals responded slower) contrasts of interest were re-examined in data aligned to response-times. In the response-aligned data there was one significantly long window of condition-related differences extending from \(-1.39 \) s before to 0.72 s after the mean decision time, \( D = 0.03 \) mm, \( t(50) = 5.12, P < 0.0005 \). In control participants there was a single significant window from \(-1.39 \) to 0.43 s after participants’ reaction time, \( D = 0.03 \) mm, \( t(27) = 3.90, P < 0.0005 \). In depressed participants, there was a significant window from \(-1.01 \) to 1.20 s after the reaction time, \( D = 0.03 \) mm, \( t(22) = 3.55, P < 0.0005 \). The response-aligned data further clarifies that condition-related differences began well before participants’ reaction time. As in the stimulus-locked data, no significant group \( \times \) condition interactions were detected at any point along the response-locked waveforms. When the data were response-aligned, the group difference in the early period was no longer significant, though the observed differences in the later period were still detectable; depressed individuals displayed decreased pupil dilation from 5.4 to 6.4 s after their responses compared to controls, \( D = 0.04 \) mm, \( t(49) = 1.82, P = 0.08, d = 0.51 \). Thus, the primary results of interest do not appear to be due to variability in reaction times.

4. Computational modeling of results
Intuitively, the results above are consistent with the notion that depressed individuals could have difficulties in selective attention because they have a harder time sustaining recruitment of cognitive resources to the tasks. Thus, once they respond to a stimulus, they are quickly distracted, or their attention decreases, which could lead to decreased cognitive load on subsequent trials. That said, the cognitive mechanism for this distraction has not yet been specified. We have previously used computational neural network models to gain insight into the time course of pupil dilation and brain activity in depression (e.g. Siegle and Hasselmo, 2002; Siegle et al., 2002). Thus, to better understand mechanisms associated with decreased sustained cognitive processing in depressed individuals we present results from post-hoc computational neural network modeling of the Stroop task.

4.1. Network construction
We adopted the Stroop model used by Cohen and Huston (1994) as augmented by Botvinik et al. (2001). This model has been shown to account for a number of salient aspects of Stroop interference including longer reaction times to incongruent words, and brain activity in areas sensitive to response conflict on incongruent trials. In addition, the model is quite similar to earlier models by Cohen et al.’s group, which have been used, in
In the past, to simulate performance by individuals with psychopathology on the task (e.g., Cohen and Servan-Schreiber, 1992). In the model (Fig. 3a), units feed a sum of their inputs, subjected to a sigmoid function, to other units to which they are connected. The model’s inputs include representations of a word and the color ink it is written in, as well as inputs to task demand units that specify whether the network is to perform color naming or word reading. Units within each layer are mutually inhibitory (i.e., have reciprocal negative weights). As detailed in Cohen and Huston (1994), a trial involves initially ‘priming’ the network with activity to the task demand units and damped outputs, followed by activity to color and word units with no response-layer damping. Activation
propagates throughout the network, and a response is said to be made when a critical threshold of activity is reached in one of the response units. As in Botvinik et al. (2001) a ‘conflict monitoring’ unit computes the product of activity in the response units as a representation of the computation performed by the anterior cingulate cortex.

Previous simulations with the network (e.g. Botvinik et al., 2001; Cohen and Huston, 1994) ended when the model generated a response. To model sustained processing after a response in the current simulations, the network was allowed to run for a longer fixed number of simulated time steps, and inputs to the task demand units were replaced with damping inputs after the response to represent disengagement after the task is completed. In addition, to simulate a brief exposure to the stimulus, input units were turned off after a brief presentation. Network parameters are included in the appendix. Because pupil dilation is conventionally thought of as a summative measure of cognitive load and because the pupil is innervated by most brain regions associated with Stroop task performance (visual cortex, prefrontal cortex, and the anterior cingulate cortex), we simulated the neural activity associated with pupil dilation by summing the mean activity in each layer at each cycle. Pupil dilation was simulated by convolving this sum with a pupillary impulse response derived from a cued-reaction time task with similar temporal features to the administered Stroop task, as in Siegle and Hasselmo (2002), which had the effect of slightly delaying and smoothing the derived time-course. Matlab code implementing the network is available from the first author upon request.

4.2. Simulating observed results

Subplots in Fig. 3B–F show the results of simulations with the network. In each graph, the X-axis represents cycles of processing through the network. The Y-axis in subplots B–E represents simulated pupil dilation and in subplot F represents the magnitude of response in the conflict detection unit. Each line represents one condition, for one simulated group. Each presented time course is the result of averaging 10 simulated runs. Standard errors were sufficiently small that all observable differences between curves may be interpreted as ‘significantly’ different. In addition to displaying the expected behavioral interference, Fig. 3b shows that the time-course of simulated pupil dilation in the network resembles observed condition related pupil dilation in healthy participants, displaying a greater peak for incongruent than congruent stimuli.

Cohen and Servan-Schreiber (1992) suggested that activity from a similar network’s task demand units is analogous to the prefrontal cortex’s role in executive control. We therefore simulated decreased task engagement by decreasing the inputs to the task demand units. As shown in Fig. 3c, this manipulation was associated with decreased simulated sustained pupil dilation relative to the simulated control group. Of note, the same manipulation also produced a small decrease in expected pupil dilation in the time directly preceding the reaction time. These data suggest that by decreasing a parameter representing cognitive control, or focus on aspects of the task, the observed group differences can be explained.

Cohen and Servan-Schreiber (1992) have also simulated prefrontal disturbances using a different mechanism. Specifically, they simulated decreased dopamine availability in the prefrontal cortex (as hypothesized to occur in individuals with schizophrenia) and showed that this manipulation led to greater behavioral Stroop interference in a similar model. Fig. 3d shows that a similar reduction in gain leads to not only increased behavioral interference but a prediction of increased pupil dilation to incongruent trials. Thus, simulating a different type of prefrontal disturbance produced a qualitatively different pattern of results than were observed in the current study, though such increased interference effects have been observed in other studies of depressed individuals, e.g. Trichard et al. (1995).

Of note, gain and task unit input manipulations did not interact (shown in Fig. 3e). Moreover, changes in no single network parameter seemed to

---

1 Inputs to the task units could be decreased tonically or phasically after the response to the stimulus to produce a decrease in simulated sustained dilation.
produce both of these phenomena. Thus, simulations suggest that disruptions in different mechanisms associated with cognitive control could be responsible for different patterns of deficits on the Stroop task.

5. Discussion

In summary, we administered a standard Stroop color-naming task to depressed and never depressed individuals using a fairly long (12 s) inter-stimulus interval and measured pupil dilation during the task. Strong but similar behavioral effects were observed in both groups; participants took longer time to name the color for incongruent than congruent trials. Similarly, pupil dilation increased after stimulus presentation and was higher for incongruent trials than for congruent trials across groups suggesting that pupil dilation represents a measure of cognitive load on the task.

Though depressed individuals did not appear to display increased behavioral or physiological measures of Stroop interference, depressed individuals did display decreased pupil dilation in the seconds following stimuli relative to controls, which was related to decreased pupil dilation on subsequent trials. Computational neural network modeling suggested that the observed effects were consistent with a disruption in prefrontal cortex function leading to decreased cognitive control. Such a decrease in cognitive control could help to explain problems with selective attention observed in depressed individuals in other experiments.

Specifically, the model suggests that decreased sustained engagement in the task could involve too little input from prefrontal cortex, i.e. decreased resources devoted to maintaining attention on the task. Such decreased attentional control could lead to selective attention deficits through a number of paths, e.g. decreased vigilance or less preparation for subsequent trials. That explanation is consistent not only with data suggesting that depressed individuals perform poorly on a host of cognitive tasks requiring prefrontal engagement (Ottowitz et al., 2002), but also with neuroimaging data suggesting that depressed individuals have decreased prefrontal activity, particularly in the dorso-lateral prefrontal region (Baxter et al., 1989; Bench et al., 1992; Drevets, 1999; Martinot et al., 1990; Siegle et al., 2002). The relationship of sustained pupil dilation in one trial to pupil dilation on subsequent trials could further support the idea that decreased cognitive engagement after one trial could reflect disengagement from the task which persists, to some extent, into subsequent trials.

These results are particularly interesting when examined in light of a broader literature in which depressed individuals have been observed to display increased sustained pupil dilation in response to emotional stimuli in multiple studies (Siegle et al., 2001, 2003a), which we have interpreted as representing sustained attention and elaboration. In fact, the same individuals who took this Stroop task also completed an emotion-identification task, and initial analyses of these data, to be published separately, suggest that the same individuals had sustained pupil dilation in response to that task. Together these data suggest that depressed individuals may display sustained engagement to emotional topics but that they have less sustained engagement in non-emotional tasks. This hypothesis could explain the common idea that depressed people have difficulty paying attention to things that are not directly relevant to them or their concerns; literally, we suggest their brain does not remain active during a task unless material is sufficiently emotional to catch their attention.

Just the same, simulations lead to a number of predictions that can be addressed by future research. Examining the time course of activity throughout, the network reveals that both simulated mechanisms affected activity in the response units as well as the task units. Thus, their product, which has been equated to anterior cingulate activity, is disrupted in a pattern similar to that predicted for pupil dilation (Fig. 3f and g). These data suggest that depressed individuals will display both prefrontal and anterior cingulate disruptions on standard Stroop tasks. The notion that two independently manipulable model parameters, both theoretically associated with disruption in prefrontal cortex, could simulate data from different populations with psychopathology also leads to a number of intriguing possibilities. Specifically, it suggests that there are multiple necessary capabilities for
The prefrontal cortex to function as the mediator of executive control.

The study had a number of methodological limitations. Foremost, the groups were significantly different in age and education. Although the difference in education was small (<1 year), the age difference was more striking. Skewed distributions prevented covarying out age in analyses but initial analyses with matched subsamples suggested that effects were not due exclusively to age; further testing with better-matched samples is still warranted. Because we used such a long inter-stimulus interval and required button presses rather than verbal responses, the task was easier than most versions of the Stroop task (e.g. as discussed by Macleod, 1992); subjects made very few errors. Thus, the generalizability of our results to understanding Stroop task performance by depressed individuals, in general, is unclear. In particular, a more difficult version of the task could have produced the types of exaggerated behavioral interference or slowed reaction times observed in other similar studies of depressed individuals (e.g. Trichard et al., 1995). Differences in reaction times for depressed and healthy individuals in the current study were of an expected magnitude (150 ms) but not reliable enough to achieve statistical significance in the current sample. A number of factors were not controlled for including the placement of the task in a larger time-consuming battery and time-of-day in testing. In addition, Guthrie and Buchwald’s (1991) technique used to identify salient windows of waveforms is insensitive to events that occur on a short time scale such as peak components; thus, the reliability of the observed group differences in early pupil dilation is unclear. The small effect size for this effect and lack of statistical significance over the entire region suggest that replication of the effect would be desirable.

The use of an unmedicated sample of depressed individuals is important in that it controls for changes in information processing that could be associated with antidepressant effects. Yet, because so many depressed individuals are given antidepressant medications, the current sample may be somewhat unrepresentative of the general population of depressed individuals.

The study is also limited theoretically, in that our claims regard brain activity, for which pupil dilation is an imperfect measure. Many factors including tiredness and the luminance of stimuli affect pupil dilation. Another important limitation is that the exact nature of the sustained processing that appears to occur in healthy, but not depressed individuals 6–8 s after Stroop stimuli is unclear. It could represent vigilance to the task, reflection on the previous stimulus, or even task-irrelevant processing. Finally, we suggest that results from the computational model should be interpreted with caution because the modeling was done post-hoc and because we have not proved that there are not other parameters or combinations of parameters that have also modeled the observed data. Thus, we suggest that further research is needed to rely on conclusions from the model.

These limitations aside, the present results do provide an intriguing basis for understanding disruptions in selective attention in depression. Specifically, they suggest that because depressed individuals’ executive control is not fully engaged during cognitive non-emotional tasks, they disengage quickly from the task after a stimulus is presented. Understanding what else is occurring for depressed individuals when they would otherwise be doing a cognitive task may thus be important to linking observed results to the phenomenology of depression. One possibility is that depressed individuals focus on personally relevant or negative information during nominally cognitive tasks; such an explanation provides a single mechanism for increased sustained processing of emotional information and decreased sustained processing of non-emotional information.

Acknowledgments

We gratefully acknowledge Roma Konecky’s and Kelly Magee’s contributions as well as the suggestions of anonymous reviewers. We thank Matt Botvinik for his code. This research was supported by MH64159, MH60473, MH55762, NARSAD, and the Veteran’s Research Foundation. This material is the result of work supported with resources and the use of facilities at the Pittsburgh VA Healthcare System, Highland Drive Division.
Appendix A: Network parameters

Parameters associated with basic Stroop effect:
Prime duration: 100 cycles
Trial duration: 400 cycles
Stimulus duration: 60 cycles
Task unit decay rate after response: random value from $-0.05$ to 0.05 per cycle
Task unit decay rate after stimulus duration: random value from $-0.05$ to 0 per cycle

Parameters associated with simulation of depression:
Task input strength: 0.7
Task unit gain: 0.8

References


