From brain imaging to intervention: Disruptions of emotional reactivity in unipolar depression

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Depressed individuals often engage in prolonged, elaborative negative thinking. This pattern is hypothesized to result from increased and uninhibited feedback between brain structures responsible for recognizing emotional features of information. This article reviews a variety of behavioral, physiological, and neuroimaging data supporting this formulation. Data suggest that depression is characterized by increased and sustained behavioral, peripheral physiological, and limbic reactivity to emotional information, as well as decreased prefrontal control, which has been implicated in inhibiting limbic regions. Neuroimaging data increasingly supports the notion that these phenomena are related: amygdala and prefrontal activity vary inversely, and this connectivity is decreased in depression. To the extent that these mechanisms are important for maintaining depression, addressing them in treatment could be useful. Thus initial efforts are reviewed examining how basic science regarding disruptions in emotional reactivity in depression can be translated to the clinic. In particular, a novel "neurobehavioral" intervention that targets brain mechanisms underlying disruptions of emotional reactivity in unipolar depression via "cognitive control training" is described.

From Brain Imaging to Intervention:
Disruptions of emotional reactivity in unipolar depression

Relationships between emotional information processing and brain function in depression are of increasing interest for a number of reasons including 1) the seriousness of unipolar depression, 2) the growing appreciation for the centrality of emotional information processing disruptions in depression, and 3) the increasing realization that understanding biological aspects of emotional reactivity in depression could aid in development of new treatments for this disorder. The first sections of this article will summarize basic research regarding emotional information processing in depression. Particular focus will be devoted to observations of increased and sustained emotional reactivity to negative information, with emphasis on examples from work being done in my laboratory. The second section will describe initial efforts at using basic research on brain correlates of disruptions in emotional reactivity in depression to guide behavioral treatment development, again, with particular focus on a specific treatment being examined in my lab.

The problem of unipolar depression

Major depressive disorder is a disabling condition that affects 7-12% of men and 20% of women across the life-time (Kessler et al 2003). Depression has been associated with impaired job functioning, disruption in
family life, and fatality. Depression is characterized by negative moods, lack of interest in pleasurable activities, feelings of worthlessness, and suicidal ideation, among other symptoms (American Psychiatric Association 1994). Each of these is intuitively related to aspects of emotional functioning and mood. As initial trials of the best validated treatments for depression, including cognitive behavioral therapy and pharmacotherapy, are effective for only 40–60% of depressed individuals (APA 2000), investigating mechanisms underlying such disruptions in mood and emotional functioning could be particularly important for better understanding and treating depression.

Sustained emotional reactivity in depression and its relationship to executive control

Some of the most troubling aspects of depression involve cognitive symptoms, such as hopelessness, pessimism, and automatic negative thoughts. These cognitive symptoms are often linked to how depressed individuals process (e.g., remember, attend to, and interpret) emotional information. In particular, depressed individuals preferentially remember negative information (Matt et al 1992), and interpret information as negative (e.g., Sullivan and Conway 1991). Increased emotional information processing biases have been associated with higher depressive severity (Matt et al 1992; Schwartz and Garamoni 1989) and the onset and persistence of depression (e.g., Beck 1967; Ingram 1984; Ingram et al 1998; MacLeod and Mathews 1991; Teasdale 1988).

Sustained involuntary elaboration upon negative information is hypothesized to underlie depressive emotional biases (e.g., MacLeod and Mathews 1991; Williams and Oaksford 1992). Such “rumination” on negative information occurs for minutes or hours after a negative thought or event (Nolen-Hoeksema 1998; Williams et al 1996). While rumination has been defined in many different ways (e.g., as concentration on symptoms of depression (Nolen-Hoeksema 1991); thinking about recent negative events (Papageorgiou and Wells 1999), or searching for meaning in salient negative life events (Fritz 1999) we have shown that nearly all formulations for rumination in depression are elevated in depressed individuals (Siegle et al 2004a). Moreover, rumination, is associated with elevated and prolonged sad mood (e.g., Nolen-Hoeksema et al 1993) and maintenance of depression (Just and Alloy 1997). Importantly, rumination and related psychological phenomena such as worry are associated with other health-related variables such as time to recover from coronary incidents (Fritz 1999), decreased heart-rate variability (Thayer and Lane 2002) & disruptions in NK cell activity (Segerstrom et al 1998).

Proposed cognitive and biological mechanisms for sustained emotional reactivity in depression

Increased cognitive feedback. Multiple cognitive theories have been proposed to explain pervasive elaboration on negative information in depression. Some of the most successful theories posit sustained feedback between mechanisms responsible for cognitive and emotional processing (Ingram 1984; Teasdale 1983). Ingram (1984) builds on the notion that cognitive activity involves nodes in a cognitive network containing
semantic information (Collins and Loftus 1975). When a node is activated (e. g., by association with an environmental stimulus) it activates nodes to which it is connected, which in turn activate other nodes. Activation thereby spreads throughout the network. Bower (1981) posited that some nodes contain emotional content. Thus, activation can occur for both the semantic and affective content of incoming information. For example, seeing a crying person might activate both “person” and “sadness” nodes in an observer’s cognitive network. Ingram suggests that people who are depressed suffer from strongly activated connections between negative affective nodes and multiple semantic concepts, creating feedback loops that propagate depressive affect and cognition. Similar frameworks have been described by other researchers to explain cognitive-emotional interactions (Metcalfe and Mischel 1999) and to account for a variety of emotional information processing data in depression (Ingram 1990; MacLeod and Mathews 1991; Teasdale 1983).

**Sustained amygdala activity.** Integrative research in affective neuroscience has lead to models that roughly parallel Ingram’s (1984) cognitive theory involving increased feedback between the amygdala system and regions responsible for other aspects of information processing. The amygdala appears important to perceiving emotional aspects of information and generating emotional reactions (e. g., LeDoux 1996). It is highly connected to cortical and subcortical regions that process other aspects of information (e. g., the hippocampus, Tucker and Derryberry 1992). Disruptions in amygdala volume and activity have been found in depressed individuals (e. g., Drevets et al 1992; Hornig et al 1997; Sheline et al 1999) and animal models of depression (e. g., Zangen et al 1999), particularly including increased and sustained amygdala activity (Abercrombie et al 1998; Drevets 1999; Sheline et al 2001; Siegle et al 2002). Such abnormalities are implicated in the maintenance of depression (Dougherty and Rauch 1997) and appear to normalize with treatment (Sheline et al 2001).

**Decreased prefrontal control.** To address sustained limbic activity in regions such as the amygdala, it is important to know not only why they would turn on in depressed individuals, but why they would not turn off. To the extent that executive control is necessary for emotion regulation (Metcalfe and Mischel 1999), and specifically, prefrontal function is necessary to inhibit limbic regions such as the amygdala (Davidson 2000; Drevets and Raichle 1998; Mayberg et al 1999; Ochsner et al 2002; Ochsner et al 2004), sustained emotional reactivity might result from decreased prefrontal executive control.

Inhibitory connections from the ventromedial and orbital prefrontal cortex (OFC) to the amygdala (e. g., Ghashghaei and Barbas 2002; Ray and Price 1993) make frontal regions strong candidates for such a “damping” mechanism. Yet, little data suggests that the medial and orbital prefrontal cortices serve a specific mood-regulatory function without initial “upstream” provocation from highly connected areas more directly involved in executive control. The dorsolateral prefrontal cortex (DLPFC), in particular, is believed to recruit brain structures used in specific tasks (e. g., Carter et al 2000) and
inhibit others. The DLPFC has been implicated, possibly indirectly through cortico-cortical connections to the OFC, in inhibiting the amygdala (e.g., Davidson 2003). Potentially then, depressed individuals suffer from decreased DLPFC activity, which indirectly allows increased amygdala activity to continue; like a car without brakes, the mechanism that would usually be responsible for inhibiting limbic processing does not become active. Further, inhibitory connections from the amygdala back to the prefrontal cortex (Amaral et al 1992; Perez-Janaray and Vives 1991) allow for the possibility that sustained amygdala activity is not only a result of, but also potentially contributes to decreased prefrontal cortex activity. This hypothesis is consistent with animal data showing that tonic amygdala activity is associated with prefrontal inhibition (Moore and Grace 2000). Thus, if the amygdala becomes active in response to an emotional stimulus, decreased prefrontal cortex activity, and hence decreased executive control function, may occur during emotional stimulation with or without endogenous decreased DLPFC function.

In support of the idea of diffusely decreased prefrontal control in depression, depressed individuals have decreased prefrontal activity compared to healthy individuals (e.g., Baxter et al 1989; Bench et al 1993; Davidson 1994; Mayberg et al 1999). Similarly, non-depressed individuals have decreased DLPFC activation in induced sad moods (e.g., Baker et al 1997; Gemar et al 1996; Liotti et al 2000). Depressed individuals also perform poorly on tasks that necessitate executive control and working memory (e.g., Ottowitz et al 2002), which engage the DLPFC (e.g., Cohen et al 1997), though this finding is qualified by age. Particularly, depressed individuals have difficulty in sustained recruitment of executive resources, e.g., on demanding sustained attention tasks. For example in a study in which participants had to say whether continuously degraded pictures of continuously presented digits were “0”s, depressed individuals’ performance decreased over time compared to controls (Egeland et al 2003). Processes that engage sustained elaborative emotional processing such as rumination also appear to interfere with cognitive tasks in depression (Watkins and Brown 2002). Finally, a plethora of literature examining resting-state EEG also suggests there is decreased left dorsal prefrontal activity in depression (Davidson 2003). Thus, despite more direct connectivity of limbic regions to the ventromedial PFC, this review will focus on the potential indirect modulatory role of dorsal lateral regions of PFC associated with executive control.

Importantly, a broad network of brain structures, systems, and neurochemical disruptions has been implicated in disruptions of emotional functioning in depression (Charney 1998; Davidson 2000; Drevets 2000; Mayberg 1997; Mayberg 2003; Phillips et al 2003). In particular, the subgenual cingulate region (BA25) has also been consistently implicated in the experience of sadness and evaluation of negative information (Murphy et al 2003), as well as depression, (Drevets 2000; Mayberg 1997; Mayberg et al 1999). In no sense is this broader conception challenged or contradicted by the relatively narrow focus of this review. Rather, this focus is intended
as a limited example of select pathways from disruptions of a few aspects of emotional information processing to specific aspects of brain function in depression.

Thus, the following sections will further consider two mechanisms for emotional information processing in depression, including increased and sustained amygdala activity, and decreased prefrontal control, specifically involving the DLPFC. The basic prediction, based on theoretical data as well as computational simulations of this system (Siegle 1999; Siegle and Hasselmo 2002; Siegle et al 2004b; Siegle et al 2002) is that depressed individuals will display sustained amygdala activity in response to emotional information and decreased DLPFC activity during both cognitive and emotional processing. A secondary prediction is that these mechanisms will be related.

Peripheral physiological correlates of sustained emotional reactivity in depression

To suggest that brain mechanisms such as sustained amygdala activity in response to emotional information are important to understanding clinical phenomena such as rumination, it is important to show that the same elaborative processes underlying rumination, on the time-course of minutes or hours following emotional stimuli, could begin in the seconds following exposure to an emotional stimulus. In fact, a great deal of evidence has related on-line behavioral and physiological reactivity to self-reported rumination (Luminet et al submitted; Roger and Jamieson 1988; Siegle et al 2003a; 2002).

Physiological correlates of sustained cognitive and emotional processing have been observed (Christenfeld et al 2000; Cuthbert et al 2000; Roger and Jamieson 1988), particularly in depressed individuals (e. g., Deldin et al 2001; Siegle et al 2001; 2003a; submitted-a). For example, depressed individuals display increased slow-wave event-related brain potentials in the seconds following presentation of negative words (e. g., Deldin et al 2001).

Thus a useful basic method for eliciting sustained emotional reactivity would involve showing depressed participants an emotional stimulus, and then waiting for a short period, and examining the extent to which sustained physiological reactivity could be observed. To examine whether executive control is important in inhibiting this sustained physiological reactivity we can present.

Assessment of pupil dilation provides a unique way of observing this relationship. The pupil dilates more under conditions of higher attentional allocation and memory use (Beatty 1982; Steinhauer and Hakerem 1992) as well as in response to increasingly affective material (e. g., Janisse 1973). For example, as individuals are asked to remember larger numbers of digits, their pupils reliably dilate (Granholm et al 1996; Kahneman and Beatty 1966). The pupil is innervated by brain structures involved in cognitive and emotional processing including the amygdala, and prefrontal cortex (Hess 1972; Koikegami and Yoshida 1953; Szabadi and Bradshaw 1996). We have specifically shown that pupil dilation is related to DLPFC activity on cognitive tasks (Brown et al 1999; Siegle et al 2003b).

When depressed individuals are asked to identify the affective valence (positive, negative, or neutral) of emotional words, they display increased and sustained pupil
dilation, a correlate of cognitive and emotional processing (e.g., Siegle et al 2001; 2003a; submitted-a). This phenomenon appears unique to negative words, at least in medicated depressed individuals (Siegle et al 2003a). Sustained pupil dilation to emotional information was significantly correlated with self-reported rumination across multiple self-report measures in that study. Moreover, sustained pupil dilation in depression does not occur in response to cognitive tasks that do not involve emotional stimuli. For example, depressed individuals display decreased pupil dilation in response to a Standard Stroop task with the same timing characteristics as the emotional information processing tasks on which they showed sustained pupil dilation (Siegle et al 2004b). This task is associated with prefrontal activity in healthy individuals (MacDonald et al 2000).

Central indices of sustained limbic reactivity in depression

Increased and sustained activity in brain regions associated with emotional processing such as the amygdala, has repeatedly been observed using neuroimaging following exposure to social and emotional stimuli. For example, Sheline et al (2001) found increased amygdala responses to masked faces in depressed, compared to control participants. We initially showed that a small sample of medicated depressed individuals displayed increased and sustained amygdala responses to negative information during an emotion identification task, which continued during a subsequent working memory task (Siegle et al 2002). This sustained amygdala activity was related to multiple self-report measures of rumination (Siegle et al 2002). Recently we have replicated these results in a larger unmedicated sample using tasks involving rating the personal relevance of emotional words and a task in which emotion-identification of words alternated with the previously described digit-sorting task (Siegle et al submitted-b).

One possibility is that the increased amygdala activity is a function of increased visual attention to presented stimuli. This is unlikely in that our recent data suggests that on the personal-relevance rating and emotion-identification tasks, depressed individuals displayed decreased activity in multiple visual cortex regions, compared to never-depressed controls (Siegle et al submitted-b).

Relationship of limbic activity to executive control

The amygdala and hippocampus were the only regions of the brain that were more active for depressed than never-depressed individuals in response to negative versus neutral information in our original sample. The DLPFC was the only brain region with relevant group differences and an inverse relationship with amygdala activity (Siegle et al 2002). This result is consistent with Deldin’s (2001) event-related potential (ERP) data in which depressed individuals displayed increased parietal, but decreased prefrontal slow-wave ERP responses to negative words in a similar paradigm. Similarly, one of the most robust results in the affective neuroscience literature is that individuals who are depressed or vulnerable to becoming depressed display asymmetric frontal alpha-band activity using electro-
encephalography (EEG) (Davidson 1998; 2000; 2003). Alpha-band EEG activity is associated with lapses in concentration or executive control; decreased left frontal EEG has been interpreted as evidence for deficits in executive control over emotion regulation. In particular, alpha EEG asymmetry has been associated with increased withdrawal-related emotional responses, compared to approach responses (Davidson 2000). Of particular note, EEG alpha-asymmetry has been shown to predict startle modulation, a measure of affective reactivity, following exposure to negative pictures (Jackson et al 2003).

These data beg the question of whether the DLPFC has a direct role in emotion-regulation. Initial data from an experiment involving passive viewing of emotional stimuli in our lab are suggestive in this regard; viewing pictures containing negative or sad faces provoked significantly greater and more sustained dorso-lateral prefrontal activity than viewing pictures containing positive or happy faces (Lee and Siegle submitted).

Thus we have begun to examine relationships between prefrontal and amygdala activity on the administered emotional tasks. Initial analyses of lagged cross-correlations on the personal-relevance rating task suggested, as expected that DLPFC activity is positively related to amygdala activity in healthy individuals, but that this relationship is decreased in depressed individuals (Siegle et al 2006b).

Thus far it is unclear whether the observed decreased prefrontal activity and connectivity on emotional tasks are simply a function of decreased prefrontal function, rather than a phenomenon specific to emotional processing. That is, though depressed patients perform poorly on tasks requiring prefrontal activity, and have decreased prefrontal activity in tasks that do not require emotional processing, these phenomena have not generally been examined in the same depressed individuals displaying increased emotional reactivity. An important exception is data suggesting that rumination specifically disrupts performance on an executive function task (random number generation) in depressed but not healthy individuals (Watkins and Brown 2002).

Our sample of unmedicated depressed individuals on average displayed both increased/sustained amygdala activity to emotional information and decreased DLPFC activity during digit sorting. These individuals also displayed both increased pupil dilation to emotional information processing tasks (Siegle et al submitted-a) but decreased sustained pupil dilation in response to a standard Stroop task with analogous timing (Siegle et al 2004b). Preliminary analyses suggest that they also displayed decreased DLPFC activity on that task. DLPFC activity during digit sorting was inversely related to self-reported rumination (Siegle et al 2006a), suggesting a potential disruption of the DLPFC's role in emotion regulation in depression. Yet, the subset of depressed individuals who displayed decreased DLPFC activity during digit sorting did not necessarily display sustained amygdala activity during personal relevance rating of emotional words (Siegle et al 2006a). These data suggest that abnormalities of amygdala and prefrontal function in depression may represent interacting, but independently
contributing mechanisms.

**From Brain Correlates of Emotional Information Processing to the Clinic**

To the extent that the previously described mechanisms are important for maintaining depression, addressing them in treatment could be useful. New "neurobehavioral" interventions that target brain mechanisms underlying disruptions of emotional reactivity in unipolar depression may thus be useful. "Neurobehavioral therapies" describe a class of interventions that address biological mechanisms believed to underlie psychological disorders, in the same sense that pharmacological and surgical treatments address such mechanisms. Yet, they use behavioral methods to do so. Neurobehavioral therapies have typically targeted aspects of prefrontal function that may contribute to disruptions in emotion regulation and reactivity in depression.

Of course, existing therapies employ techniques that could increase cognitive control. For example, cognitive therapy teaches patients to consider evidence that does not support their automatic thoughts, rather than engage in more automatic ruminative processes. "Mindfulness based” therapies directly target attentional allocation (Segal et al 2001). Indeed, neuroimaging following pharmacological and behavioral interventions has demonstrated associations of increased prefrontal, activity with recovery from depression (Davidson et al 2003; Liotti and Mayberg 2001; Liotti et al 2002). Yet, it is unclear whether recovery or changes in brain function in these interventions is due specifically to increased cognitive control.

The difference in neurobehavioral therapies is that they are designed with specific biological mechanisms in mind. Thus they often appear different from conventional psychological treatments designed to address observable symptoms or cognitive or behavioral manifestations of underlying mechanisms.

A number of neurobehavioral therapies for depression are currently being examined. For example, as previously discussed, prefrontal EEG alpha-asymmetry is a hallmark of depression associated with poor emotion regulation. EEG asymmetry has consistently been associated with disruptions in prefrontal cortex function (e. g., Davidson 2003). In “neurofeedback”, electroencephalogram (EEG) biofeedback is used to help participants to monitor and manipulate the activity of relevant aspects of brain function on-line. Initial neurofeedback approaches to depression have involved regulation of alpha-asymmetry (Baehr and Baehr 1997; Baehr et al 1997; Rosenfeld et al 1996). Similarly, a growing literature suggests that depression is characterized by deficits in prefrontal brain function associated with behavioral inhibition, activation, and goal pursuit. In response, Strauman et al (submitted) have created a “Self-System” therapy, a brief structured intervention intended to improve self-regulation in service of goal attainment. The therapy involves teaching and practicing specific skills e. g., initiation of goal-promotion focused behavior, explicit goal evaluation, and restoring effective self-regulation. Strauman's group is currently using fMRI to understand whether brain function associated with goal pursuit and self-regulation changes as a result of the
My lab has evaluated a specific type of neurobehavioral therapy stemming from the cognitive rehabilitation literature. Cognitive rehabilitation is devoted to remediation of neurological insults, through exercises that affect and increase function in either areas that have been damaged, or in surrounding regions that may be useful in compensating for injuries (e.g., Christensen and Uzzell 2000; Parentàe and Herrmann 2003; Riddoch and Humphreys 1994; Sohlberg and Mateer 2001). Cognitive rehabilitation begins by identifying affected cognitive functions and brain regions. Repetitive behavioral exercises are employed to strengthen aspects of cognition thought to be subserved by affected brain regions. Cognitive rehabilitation has successfully been applied to post-stroke complications, memory disorders, and other brain-injury derived psychological conditions, and addresses many cognitive functions disrupted in depression such as attention, memory, and cognitive organization. Improved mood (i.e., decreased dysphoria) has, in fact, been observed following similar cognitive rehabilitation interventions for other disorders such as Multiple Sclerosis that employ prefrontal-cortex-intensive neuropsychological tasks (Allen et al 1998). The success of these methods suggests that behavioral exercises may show promise in addressing often similar disruptions of brain function associated with other psychological disorders.

In particular our intervention targets disruptions of prefrontal function that could contribute to sustained emotional reactivity in depression. The theory is that by increasing prefrontal function, particularly in the face of stressful emotional reactions, decreased prefrontal activity that leads to increased limbic dysregulation could be corrected. The basic approach is to exercise depressed individuals repeatedly on two tasks that require prefrontal activity to complete.

The first task exercises prefrontal function in the context of likely negative automatic ruminative cognitions and is based on Wells's (2000) Attention Training. This task requires individuals to learn to direct their attention. Participants are instructed to focus on one sound at a time occurring in a naturalistic environment; they focus on only that sound, which exercises selective attention processes. Then participants are asked to switch attention between the sounds and count the sounds, all the while, staying focused on the task rather than naturally occurring depressive ruminative thoughts. In this way, the task not only exercises selective attention to specific environmental stimuli, but cognitive control is needed to stay with the task rather than more automatic emotional processes. The protocol, takes approximately 15 minutes per session. Such an intervention could be seen as useful in helping depressed individuals to regain cortical control of otherwise automatic emotional processes. Intuitively, this therapy may be considered one form of neurobehavioral treatment for prefrontal cortex dysfunction. This protocol has been studied extensively in anxiety disorders; an initial study suggested the intervention was useful in treating four depressed individuals in just a few sessions (Papageorgiou and Wells 2000). Our group has created a computer-administered
version of the protocol. Bird sounds (from Blinkow 1999), presented in four-speaker surround sound at randomly occurring intervals, provide the environmental stimuli.

The second task requires prefrontal control and use of working memory in the presence of some emotional reactivity (in this case, slight frustration), so that prefrontal function is required in the presence of likely amygdala activity. Towards this end, we used a variant of the Paced Auditory Serial Addition Task (PASAT, Gronwall 1977), which involves continuously adding serially presented digits in working memory. Participants are asked to add each new digit to the digit that preceded it (i.e., sum just these digits, and not keep a running sum). Difficulty is manipulated by increasing the speed with which items are presented. Participants are instructed to get as many items right as they can and to resume the task as quickly as possible when they get something wrong. Thus, the task not only taps working memory, but executive control. A recent study in which nine healthy individuals completed the PASAT during assessment with fMRI reported that left middle frontal gyrus activity (including the DLPFC) was increased during the PASAT vs. a control task (Lazeron et al 2003). Further, depressed individuals have been shown to score lower than controls on the task (Landro et al 2001), even when performance on other neuropsychological tasks was controlled for. The PASAT is known to be frustrating (Holdwick and Wingenfeld 1999). Thus, to keep the task tolerable by depressed participants (i.e., control induced frustration on a per-subject basis), likely to engage prefrontal circuitry rather than a “giving up” reaction, and likely to remain a useful exercise even after training, a modified version of the task was used that adapted to participants’ performance. This version begins at a 3000ms inter-stimulus interval (ISI) and speeds up by 100ms when participants get four consecutive items correct. It slows down by 100ms when they miss four consecutive items, to keep participants at a constant level of performance. This technique equates the task for difficulty across participants and sessions. Participants completed three 5-minute blocks per session. An adaptive variant of the PASAT has previously been used; the speed of presentation on the task was positively correlated with performance on other tests of executive function (Royan et al 2004).

We have recently reported a preliminary trial of this intervention (Siegle et al in press). Thirty-one severely depressed outpatients received treatment as usual in the Intensive Outpatient Program at Western Psychiatric Institute and Clinic, including medication management, supportive group psychotherapy based on the principles of dialectical behavior therapy (Linehan et al 1993), and milieu therapy. Of these 31 patients, 19 also received six sessions of the Cognitive Control Training (CCT) intervention, involving the two tasks we have described, in the first two weeks of treatment. All patients completed diagnostic interviews and assessments of cognitive and emotional information processing before and after the intervention during physiological or neuroimaging assessment.

Results suggested that depressed patients who received CCT experienced...
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greater decreases in depressive severity and self-reported rumination compared to those in treatment as usual (TAU). Their symptoms and rumination scores declined linearly with each CCT session. Their performance on the adaptive PASAT also increased each week, suggesting that they were improving on a prefrontal task in the intervention. The group who received CCT experienced greater improvement in performance on a non-adaptive version of the PASAT compared to the TAU group. In particular they recovered more quickly from errors, potentially suggesting that training on cognitive tasks allows increased regulation, or at least recovery from negative emotions such as frustration.

Finally, the six patients who completed CCT and were assessed with fMRI before and after CCT experienced decreased amygdala activity following exposure to negative words, and increased amygdala activity to positive words. In addition, patients displayed increased DLPFC activity on the digit sorting task, potentially suggesting that the intervention was associated with decreases in brain correlates of emotional reactivity, and increased prefrontal function.

The remaining 25 patients were assessed using pupil dilation as a measure of cognitive and emotional load on tasks requiring emotional information processing. These data suggested that depressed patients displayed decreases in sustained pupil dilation on both the previously described personal-relevance-rating and emotion-identification tasks. Importantly, participants in the TAU group also displayed similarly decreased pupillary reactions suggesting that observed changes in brain function could be general to recovery from depression, and not restricted to change in this particular intervention.

Of final note, both patients and their clinicians in the Intensive Outpatient Program were uniformly enthusiastic about the intervention. For example, subjects stated, “The ‘birds’ intervention... helps me to focus on just the sounds and not what thoughts keep recurring like traffic I was in to get to my appointment, etc,” “I have been ruminating about past events less,” and “When I'm doing the puzzle I can think about nothing but the puzzle. I wasn’t able to do this as much before. There was a constant barrage of thoughts that would interrupt what I was doing.”

Summary

In conclusion, the fields of affective neuroscience and depression research are increasingly convergent. Disruptions in aspects of brain function associated with automatic emotional reactivity could translate to behavioral disruptions in mood and sustained elaboration of negative information, in the form of rumination. Deficits in executive control could contribute to, and be exacerbated by these disruptions in emotional information processing. Novel behavioral interventions that explicitly target these brain processes are promising, and could lead to new ways of understanding and addressing this pervasive disorder.

Author Note

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Lee KH, Siegle GJ (submitted): Different BOLD responses to emotional faces and emotional
faces augmented by contextual information.


Siegle GJ, Steinhauer SR, Carter CS, Thase ME (submitted): Is sustained processing specific to emotional information in depression? Evidence from pupil dilation.


要約

脳画像から介入へ—単極性うつ病における感情反応性の障害—

うつ病の個人は、しばしば持続的で没入的な否定的思考を含む。この傾向は、情報の感情的特徴を認識する脳機能の間、増強され、抑制が効かないフィードバックによってもたらされると仮定される。本論文では、この仮説を支持する、行動的知見、生理的知見、神経画像の知見を概観する。それらの知見は、うつ病の特徴は、感情的情報への増強された持続的、行動的、仮想生理、辺縁系活動の反応性、さらに辺縁系領域を抑制すると考えられている前頭前野によるコントロールの低下であることを示唆している。神経画像の知見は、それら2つの特徴が関連していることを示している。すなわち、扁桃体と前頭前野の活動は拮抗的であり、うつ病の個人においては、それら2部位の結合性が低下している。それらのメカニズムがうつ病の維持において重要であるとすれば、そうした問題を検討することは治療のために有益であろう。そこで、うつ病における感情反応性の障害に関する基礎的研究が、どのように治療場面へ応用できるかに関する、始まったばかりの試みを概観する。特に、新しく考案された、単極性うつ病における感情反応性の障害の脳内メカニズムを対象にした、「認知コントロール訓練」による「神経行動的」介入について紹介する。

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