Effort and Cognition in Depression

Robert M. Cohen, MD, PhD; Herbert Weingartner, PhD; Sheila A. Smallberg; David Pickar, MD; Dennis L. Murphy, MD

Motor performance and cognitive function were examined in depressed patients and controls. Increasing severity of depression was strongly associated with decrements in performance in both motor and memory tasks. Greatest depression-related impairment was found on those cognitive and motor tasks that required sustained effort. We discuss these results in terms of a generalized deficit in the central motivational state of depressed individuals.

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Cognitive changes frequently accompany the mood disturbances that characterize the affective disorders.1,2 Laboratory observations of depressed patients show a positive correlation between the degree of memory impairment and the intensity of depression.3-5 However, the mechanisms and structure of cognitive changes in depression remain poorly understood6 (R.M. Cohen, MD, PhD, et al, unpublished data, May 1978). The difficulties are due both to a lack of systematic exploration of depression-related cognitive mechanisms and the uncertainties in our understanding of unimpaired cognition.

These latter uncertainties arise in part from a failure of staging theories of information processing to adequately differentiate the components of memory and learning, eg, attention, short-term memory, long-term memory, retrieval, and memory consolidation.6-8 In place of staging theories, new strategies have emerged that emphasize the context for processing an event, the characteristics of the to-be-remembered stimuli, and the elaborateness of the operations performed by the subjects as determinants of whether an event is memorable.9-10 This "single trace" conceptualization of information processing has been increasingly useful and productive in the study of learning and memory.

Within this theoretical framework, investigators have devised strategies for manipulating the activity or effort required of experimental subjects to successfully complete cognitive tasks. Specific cognitive operations are classified somewhere along the continuum between active and passive.10,23-27 Passive or automatic operations are defined in part by their capacity to be carried on simultaneously with little cost in their performance. In contrast, tasks that involve effort or active processing require some sustained motivation, are more easily disrupted, and are not independent of other operations that also require effort. As currently conceptualized by some researchers in this area, automatic processes appear to be "wired in" and species specific, whereas effortful processing appears to involve more individual variation between and within subjects. This distinction between effortful and passive or automatic processing of information may be used to conceptualize strategies for defining the cognitive impairments in depression. For example, the degree of arousal and mood state are considered influential determinants primarily of effortful processing.

Both social-learning and cognitive-behavioral theory have considered the mechanisms by which reinforcement, drive, and motivation might mediate environmental or stimulus-specific performance so as to produce behavioral decrements in depressed individuals.28-31 Although changes in these conceptually related variables, particularly in drive and motivation, have been observed in depression, few attempts have been made to systematically explore and integrate these findings with specific memory deficits. In this study, we examined whether a general deficit in the central motivational state in depression could account for the memory impairments observed in depression. We proposed that the depressive's reduced capacity to integrate external stimuli with appropriate behavioral response, or the maintenance of such a response, would result in an increasing decrement in his cognitive performance as the effort required of him increased. To test this hypothesis, a simple motor task was devised that would provide a measure of effort that was relatively independent of both intrinsic motor strength and cognitive processing. The subjects of the motor task would also be expected to perform a simple memory task requiring little motor activity. The two tests would permit direct comparisons between individual (motor) effort and cognitive performance.

SUBJECTS AND METHODS

Subjects

Subjects for the study consisted of normal volunteers (mean age, 37.2 years; SD, 15.5 years; range, 19 to 53 years) and patients with affective disorders (mean age, 33.2 years; SD, 11.7 years; range, 20 to 50 years) living on a research unit at the Clinical Center of the National Institutes of Health, Bethesda, Md. Two of the volunteers were also housed on the same unit during the period of the study. The remainder of the volunteers were chosen from among the nonprofessional staff of the institution. All subjects had at minimum completed a high school education. Educational levels of volunteers and patients were roughly comparable. The diagnosis of major affective illness in each of the patients was made on the basis of Research Diagnostic Criteria,27 with the aid of the Schedule for Affective Disorders and Schizophrenia.32 Two female patients reached criteria for bipolar II subtype. All other patients were of the unipolar subtype and in varying stages of their illness during testing. During the three-month study interval, all patients who were drug free for at least three weeks as part of a placebo period were asked to participate. Each subject was fully informed about the nature and purpose of the experimental tasks and gave his informed consent to participate. The patients received a weekly Hamilton Depression Scale rating by a physician, and were rated twice a day by the nursing staff utilizing the Bunney-Hamburg 15-point ward rating scale.33 Beck Depression Inventories were obtained from patients weekly, and each subject completed a Profile of Mood State (POMS) prior to each motor test.34 Motor tests were administered in the mornings and memory tests in the early afternoon.

Procedure

For the motor task, each subject was instructed to squeeze a dynamometer, which had been placed on a table in front of him, as hard as he could, first with his right hand and then with his left.
Following the recording of each peak response in kilograms, the subject was requested to squeeze the dynamometer again. This time, the subject was informed that he was only to squeeze hard enough to reach half his previous maximum, and then to maintain this pressure for as long as possible. To accomplish this, since he was unable to view his own performance, he was instructed to slowly increase the pressure he was exerting until the tester informed him that he had reached half his peak response and then to maintain this squeeze as long as he could. Sustained time was measured from the point the subject reached half his maximum and ended when the observed hand pressure dipped 5% below the half-maximum mark.

The memory task used equivalent lists of 40 trigrams. Each trigram or nonsense syllable consisted of three different consonants. The lists were randomly assigned to the subjects. This test was controlled for pronounceability, meaningfulness, and frequency of occurrence. The choice of trigrams as stimuli, or target items for learning and recall, was predicated on the fact that subjects had to be tested frequently with material that was easily forgotten and would not be likely to produce either facilitating or inhibiting effects with repeated usage. Also, comparative performance on this task has been evaluated in samples of unimpaired subjects ranging in age from 19 to 52 years. These evaluations have provided normative findings for this study as well as other investigations, including drug-induced impairments in learning and memory.\(^6\) As the task was performed, the subject was instructed that the experimenter would read aloud a single trigram. At one of five (0, 3, 6, 9, or 18 s) different times (randomized for order) after trigram presentation, he was asked to recall the trigram. After recall of the first, a second trigram was presented in this manner (eight trigrams for each interval) until all 40 trigrams on the list for that day's trial had been presented and recall attempted. As a short distractor task designed to prevent rehearsal during the intervals between presentation and recall, the subject was instructed to count backwards from 200 by threes. Test scores consisted of the number of trigrams recalled at each interval, with a score of 8 reflecting a perfect performance for that interval.

The study was originally designed to measure both intersubject and intrasubject changes in motor and memory performances as related to mood shifts. However, based on clinical judgment and confirmed by our objective assessments of mood state, no subjects in the study showed substantial mood change while drug free. It was therefore possible to collect all of each subject's performances on the motor and memory tasks as well as the corresponding ratings for the entire period and average them to obtain a single mean value for each subject. This avoided the introduction of any bias as a result of variable subject participation. First sessions were taken as practice and eliminated from further analysis. A total of 80 memory and motor tests were obtained from the 11 individuals in the depressed patient group while drug free, and 11 from the five individuals in the normal control population. No subject was tested more frequently than once every two days. As expected, no trend was observed for change in any individual subject across his motor and memory tasks during the period of testing.

F ratios obtained for both linear regressions and analyses of variance (ANOVA) were judged significant whenever the corresponding P value was equal to or less than .05.

**RESULTS**

Initial evaluation made use of straight-line regression analyses of variables derived from the behavioral ratings, motor, and memory performances. Further evaluation used an ANOVA model in which subjects were categorized into groups of severely depressed patients (five women, aged 19, 31, 34, 53, and 60), moderately depressed patients (three women, aged 21 [bipolar II], 24, and 53), euthymic patients (one woman [bipolar II], aged 66; two men, aged 23 and 35), and normal controls (four women, aged 20, 33, 38, and 50; one man, aged 25). The total population for all the statistical analyses was 16, with the exception of comparisons that used the Hamilton or Beck rating scales. As monitored subjects did not receive these more clinically oriented and symptom-based scales, their total population was 11.

**Correlational Analysis**

The consistency of the patient behavioral ratings was underscored by the significant correlations between the subjective and objective rating scales, eg, the POMS Depression Scale (POMS-D) with the Hamilton (r = .92, P = .001) and Beck (r = .97, P = .0001), and the Beck with the Hamilton (r = .92, P = .001). As they were so highly correlated, it is possible to report correlations between mood and motor and memory performances in terms of the POMS-D as representative of the data as a whole. The motor tasks also demonstrated similar consistency. Left-hand and right-hand peak responses were significantly correlated (r = .95, P = .0001), as were left-hand and right-hand sustained performances (r = .77, P = .0004). A somewhat lower correlation was found for right-hand peak with right-hand sustained response (r = .65, P = .006), while left-hand peak vs left-hand sustained response was not significantly correlated (r = .45, P = .08).

All behavioral ratings had significant negative relationships with respect to motor performance. The POMS-D was significantly negatively correlated with peak motor responses (right hand, r = -.63, P = .009; left hand, r = -.56, P = .02) and even more highly negatively correlated with sustained motor performance (right hand, r = -.66, P = .006; left hand, r = -.73, P = .001). Similar correlations were obtained with the Beck and Hamilton depression scales.

Next, the relationship between mood and memory performance was examined. Memory performance was observed to be inversely related to the behavioral rating scales. The POMS-D ratings were significantly negatively correlated with the number of words recalled immediately (r = -.82, P = .0001), at 3 s (r = -.77, P = .0005), at 6 s (r = -.75, P = .0007), at 9 s (r = -.53, P = .035), and at 18 s (r = -.76, P = .0006). Again, the other depression rating scales yielded similar negative correlations.

Finally, motor and memory performance were contrasted. Performance on all motor tasks was positively correlated with the number of trigrams recalled at each recall interval, with correlation coefficients ranging from .42 to .72 and with corresponding significance probabilities of .01 to .002. In general, high correlations with recall were observed for right- and left-hand sustained motor performances; for example, when recall at the longest interval was correlated with right- and left-hand motor responses and right- and left-hand sustained motor responses, correlations of .56, .49, .66, and .62 were obtained, respectively.

**Subgroup Analysis**

Table 1 summarizes the mood data for the subjects as they were divided into groups of normal, euthymic, moderately depressed, and severely depressed subjects on the basis of the POMS-D scale. As a reflection of the meaningfulness of this division, one-way ANOVA using the Hamilton, Beck, and POMS-D scales as dependent variables demonstrated significant group differences (F[2,7] = 13.08, P < .01; F[2,6] = 54.3, P < .001; F[3,12] = 63.3, P < .001, respectively). Significance was not observed for right- and left-hand peak motor performances across the four subject groups, although a trend was evident (right-hand peak, F[3,12] = 2.7, P = .09; left-hand peak, F[3,12] = 2.2, P = .14). However, significant differences among groups were found for sustained motor performance (right hand, F[3,12] = 21.58, P < .001; left hand, F[3,12] = 7.54, P < .001), and memory performance (F[3,12] = 10.82, P = .001) (Table 2).

These findings of a reduction in the sustained motor...
performance according to severity of depression ratings are particularly striking in that the output of effort for each individual would be expected to be a function of both peak and time. Despite the reduction in peak, the depressed subjects still cannot hold at half maximum as long as normal subjects. As for the memory tests, there was as expected a significant time effect, ie, number of words recalled was decreased as the time between exposure and recall was increased \( (F[4,48] = 1.99, P = .047) \). As evident in the Figure, it is the severely depressed subjects' performance that most rapidly decreases with time of recall as compared with the other three groups.

**COMMENT**

The results demonstrate deficits in the motor and cognitive performance of depressed patients that appear to be proportionate to depression severity. On the motor task, depressed patients had both a reduced capacity to exert maximally and an inability to sustain their half-maximal hand squeeze as measured by our dynamometer procedure. On the memory task, the depressed patients recalled fewer trigrams at all recall intervals. The impairment on both motor and cognitive tasks appeared to be most noticeable on those subtasks that required greater sustained effort. For example, increasing the length of time over which a subject must retain three consonants in memory before recall would be expected to increase the effort required of the successful subject. Thus, the observed increase in recall deficit in depression with increasing time is consistent with the hypothesis of an enhanced deficit in the depressed subject on those tasks requiring the greatest effort.

Several objections might be raised as to the generalizability of these observations. The first is that the findings result from studies predominantly in female subjects, eg, there are no men in the severely depressed group. The second is the potential long-term effects of psychotropic medications that the patients may have been receiving before their drug-free period. Third, the data are based on group phenomena only, with a small number of subjects. In support of generalizability, we had, in fact, tested one severely depressed man (POMS-D score, 60; Beck score, 57; Hamilton score, 54); however, because we were unable to obtain memory data from a drug-free period, he was not included in the analysis. His data do, however, support the notion of a decrease in effort; six motor trials averaged a right-hand peak of 39 kg, left-hand peak of 26 kg, a right-hand sustained response of 3.0 s, and a left-hand sustained response of 2.0 s. In addition, we have had more than an equal number of motor and memory tasks completed by patients while receiving drugs, and although the number of drugs were sufficiently diverse as to preclude detailed statistical analysis, there was no trend for any of the patients receiving tricyclic antidepressant drugs to have shifts in either their memory or motor performances when no mood response was evident. Finally, we have recently retested one patient from the severely depressed group who has had a considerable clinical improvement while receiving nortriptyline hydrochloride. As expected,

### Table 1. Depression Scale Ratings for Patients With Affective Disorders and Normal Controls

<table>
<thead>
<tr>
<th>Profile of Mood State</th>
<th>Depression Subscale</th>
<th>Hamilton Depression Scale</th>
<th>Beck Depression Inventory</th>
</tr>
</thead>
<tbody>
<tr>
<td>Depressed patients</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Euthymic</td>
<td>8.5 ± 1.5</td>
<td>11.1 ± 5.8</td>
<td>4.4 ± 2.3</td>
</tr>
<tr>
<td>(N = 3)</td>
<td>(6.3-10.5)</td>
<td>(5.3-16.9)</td>
<td>(2.0-6.7)</td>
</tr>
<tr>
<td>Moderate</td>
<td>21.5 ± 1.6</td>
<td>21.9 ± 7.6</td>
<td>20.3 ± 7.1</td>
</tr>
<tr>
<td>(N = 3)</td>
<td>(20-24)</td>
<td>(10-40)</td>
<td>(10-30)</td>
</tr>
<tr>
<td>Severe</td>
<td>52 ± 4.0</td>
<td>44.6 ± 4.4</td>
<td>44.9 ± 2.3</td>
</tr>
<tr>
<td>(N = 5)</td>
<td>(39-66.8)</td>
<td>(40-52.8)</td>
<td>(39.7-46)</td>
</tr>
<tr>
<td>Normal controls</td>
<td>7.5 ± 2.7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(N = 5)</td>
<td>(2.5-14.5)</td>
<td></td>
<td></td>
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</tbody>
</table>

*Mean values ± SEM; ranges are indicated in parentheses.

### Table 2. Motor and Memory Performances by Patients With Affective Disorders and Normal Controls

<table>
<thead>
<tr>
<th>Force Exerted by Subjects, kg</th>
<th>Duration of Half-Maximal Response, s</th>
<th>No. of Trisyllables Recalled†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Right-hand Peak</td>
<td>Right-hand Sustained</td>
<td>Left-hand Sustained</td>
</tr>
<tr>
<td>Depressed patients</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Euthymic</td>
<td>42.2 ± 15.7</td>
<td>17.2 ± 2.7</td>
</tr>
<tr>
<td>(N = 3)</td>
<td>(35.6 ± 16.4)</td>
<td>(24.5 ± 0.7)</td>
</tr>
<tr>
<td>Moderate</td>
<td>25.0 ± 0.8</td>
<td>9.4 ± 1.7</td>
</tr>
<tr>
<td>(N = 3)</td>
<td>(19.3 ± 1.7)</td>
<td>(17.9 ± 7.8)</td>
</tr>
<tr>
<td>Severe</td>
<td>22.2 ± 1.0</td>
<td>9.5 ± 2.0</td>
</tr>
<tr>
<td>(N = 5)</td>
<td>(19.8 ± 0.9)</td>
<td>(8.4 ± 2.0)</td>
</tr>
<tr>
<td>Normal controls</td>
<td>42.2 ± 8.5</td>
<td>25.1 ± 1.4</td>
</tr>
<tr>
<td>(N = 5)</td>
<td>(35.3 ± 6.7)</td>
<td>(28.6 ± 3.1)</td>
</tr>
</tbody>
</table>

*Mean values ± SEM.
†Derived by averaging number of trigrams recalled at each time interval (0, 3, 6, 9, and 18 s).
her performance on both the memory and motor tasks strikingly improved.

We therefore believe that these results support the hypothesis of a general deficit in the capacity to maintain effort as an important component for the understanding of the cognitive and other behavioral changes that take place during depression.

**Studies of Model States**

This "lack of effort" on the part of depressed patients has been frequently observed by clinicians, who have noted their increased dependency, indecisiveness, and avoidance of responsibility as part of a general picture of motivational change. So striking are these changes that they are sometimes accorded a central role in models of depressive illness, eg, Schmale and Engel's37-39 conservation withdrawal or "giving up—given up" and Miller and Seligman's40 "learned helplessness" animal model. The latter model deserves detailed attention in view of our own results and the extensive behavioral and neurochemical investigations associated with the model.

The Miller and Seligman hypothesis is based on a body of work in which animals demonstrated deficits in their performance and learning of active avoidance behavior after inescapable but not escapable shock. The original investigators proposed that the animals had learned the concept that nothing they did mattered.41-42 Subsequent work in other species, however, has cast considerable doubt as to the necessity of postulating a mediating cognitive concept to explain the deficits observed.

For example, Weiss et al42-43 in recent reviews have offered an alternative explanation in which the stress-induced physiological changes result in a problem with "motor activation" that accounts for the observed performance deficits. Consistent with their hypothesis, deficits depend on the amount of motor effort required in the active avoidance paradigm. On the neurochemical level, the effects have been proposed to depend on the reduction in brain catecholamine levels demonstrated to follow inescapable shock.44-47 As expected, then, these specific behavioral effects have been mimicked, enhanced, or alleviated experimentally by drug treatment. Dopamine antagonists, catecholamine blocking agents (eg, FLA 63, alpha methylparatyrosine) or increasing cholinergic activity have been demonstrated to exacerbate the syndrome, and levodopa or cholinergic antagonists antagonize these effects.48 Most importantly, prior escape training leads to resistance to the drug- or stress-induced effects. These observations find their parallel in the cognitive depression literature. Levodopa and amphetamine enhance memory performance in depressives.49-50 Practice of otherwise effortful processes would be expected to move cognitive processes along the continuum toward the automatic end of the spectrum, making them less susceptible to changes in central motivational state.50-52,54,55 Particularly striking in terms of the maintenance of effort concept are the observations that affected animals often show normal performance on initial trials but fall off when responses are measured over additional trials.56

Considerable additional evidence exists to link these changes in catecholamine pathways to affective pathol- ogy mood states and with motivation, arousal, reinforcement, and learning in animals.59-60 Other transmitters and hormones (eg, opioid-like peptides, corticotropin, vasopres- sin, cortisol), however, have also been implicated in memory processes and mood changes.59-60 Therefore, which specific pathways are associated with the specific motivational and cognitive changes observable in depression still remain to be determined. Furthermore, whether these observed motor effects in animals originate from a more general problem involving the reinforcement, motivational areas that would be expected to be actively involved in the maintenance and initiation of all behavior, as is suggested by the "learned helplessness" hypothesis, is at present unknown.

**Observations in Depressed Patients**

In this context, however, the observations in the depressed patient population take on additional significance. Cognitive performance in general requires little motor activation or effort, and simple motor tasks require little in the way of cognitive process. If the decrements in performance of both motor and cognitive functions in depression show a close relationship, as we have observed, the most parsimonious explanation would be one based on a single deficit in the area of the central motivational state.

For example, in the specific case of memory tasks, which require the recall of words, there is evidence to support the hypothesis of an initial automatic activation process resulting from a word being read aloud.23 However, many of the alternative strategies or responses that are normally activated to obtain the goal of memorizing specific types of materials are unobservable and even subjectively unappreciated. All of these tasks would be expected to require extended effort and therefore be affected by arousal and mood.

Observations on the importance of these encoding processes in impaired and unimpaired cognition must, however, rely on indirect measurements of their participation in observable memory performance change resulting from the manipulation of stimuli. For example, Weingartner et al49 recently established a differential response of depressed patients to the varying task requirements of memorizing lists that varied in organization. Depressed subjects perform essentially as normal subjects for highly clustered and organized material, but fall off sharply when more effortful encoding strategies are required. As predicted by this model, depressed and nondepressed college students perform equally well on frequency estimates, but depressed patients perform less advantageously when mnemonic activities such as semantic processing are involved.29 Depressed patients also show a greater deficit in free recall in comparison with cued recall, the former task requiring probably greater depth of processing and therefore effort in learning and/or a greater effort in the use of a more complex retrieval strategy.

**CONCLUSIONS**

These findings raise considerable doubt as to the reasonableness of hypothesizing specific memory deficits in depression separable from the general deficits of motivation, drive, and attention. Rather, wherever one might look in terms of cognitive deficiencies, regardless of stage or process (eg, attention, short-term memory, long-term memory, consolidation, retrieval), one is likely to find factors susceptible to deficit in the depressive patient, if one is free to vary the requirements of the tasks in such a manner as to increase the complexity and therefore the effort required of the subject. Consequently, the study of the specific memory deficits in depression may disclose important information about the more general problems of initiation and maintenance of behavior in the depressive state. In addition, such study may serve to demonstrate the specific sites for the physiologic and neurochemical substrata influencing the interaction of the central motivational state with the specific processes that are part of memory. However, it must be emphasized that the specific
hypothesis of a unifying single deficit in the area of the central motivational state for depression is only one of many alternative hypotheses that could reasonably be proposed to explain depression-associated performance decrements.

Eberhard H. Uhlenhuth, MD, discussed with us the subjects of refinement and cognition.

References

31. Eberhard H, Hagerstown, Md, Harper