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IS THERE A COGNITIVE MARKER IN MAJOR DEPRESSION?

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The purpose of this study was to compare adolescents' response pattern on specific visual tasks during acute and recovered states of depression. Twenty-three inpatient adolescents with unipolar depression were tested before and four weeks after treatment. Twenty control subjects matched in age, sex, handedness, and intelligence were tested at similar intervals. Measures included four visual spatial tasks: the Gestalt Street Completion Test, the Judgment of Line Orientation, the Hooper Visual Organization Test and the Rey-Osterrieth Complex Figure. Overall, the results indicated that depressed adolescents performed significantly more poorly than controls in all four measures during both pre-and posttest conditions. They demonstrated greatest difficulty in measures of Gestalt Closure and Judgment of Line Orientation. However, the Gestalt Closure task was the only one to be correlated to severity of depression. These findings are discussed in the light of previous research suggesting a right hemisphere dysfunction and the existence of a cognitive marker in affective disorders.

Keywords: neuropsychology, depression, visuospatial deficits, cognitive marker

The evidence supporting the biological theory of affective disorders has increased and indicates: (a) that there is a genetic influence which is more pronounced in bipolar than in unipolar patients (Hauge, Harvald & Fisher, 1968; Bertleson, Harvald & Hauge, 1977; Kety, 1979; Zerbin-Rudin, 1980; Perris, 1982; Nurenberger & Gershon, 1984), and that a predisposing environment, genetic factors, or both are necessary for the disorder to be expressed (Egeland, Gerhard & Pavis, 1987); (b) biochemical and cytopathological studies suggest that for the occurrence of major depression coexisting abnormalities of multiple neurotransmitter systems may be required (Aston-Jones, Foote & Bloom, 1984; Janowsky, et at., 1981; Sitaram, et al., 1980) and be reflected in the types and severity of symptoms which result, and in turn may be appropriately responsive to different types of pharmacological or other forms of treatment (Zubenko & Moossy, 1988).

The question whether affective disorders are associated with mild brain alteration has stimulated numerous Computed Tomography studies. Schlegel and Kretzschmar's review of the literature (1987) indicated that, when compared with controls, there is an increased lateral ventricular size in unipolar and bipolar patients with psychotic symptoms; however, it was unclear whether ventricular enlargement is the result of multiple psychotic episodes or a preexistent risk factor for depressive delusional symptoms.

The idea that cerebral dysfunction could be a marker for psychopathology arose from the fact that structural and functional disorders may mimic each other's symp-

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toms. Flor-Henry (1969) made one of the first arguments in favor of applying the model of hemispheric specialization in the understanding of psychopathology. He based his arguments within a context of the study of behavioral and emotional manifestation of focal epilepsy. He found that epileptic patients who had either bilateral or left temporal lobe focus manifested schizophrenic-like psychosis; whereas, those with right temporal focus were more likely to display an affective disorder.

There have been different approaches investigating the relationship between hemispheric functioning and affective disorders. Some have studied the incidence of affective symptoms with patients with known brain lesions (e.g., Flor-Henry, 1969; Goldstein, 1939). Others have used brain imaging techniques (e.g., Wexler, 1988: Shaffer, Davidson & Sharon, 1983), and neuropsychological assessment to compare patients with affective disorders with other psychiatric patients and normal subjects (e.g., Cassens, 1988; Flor-Henry, 1983).

The data on the lateralization of emotions comes from various sources. Early reports of the affective consequence of brain damage (Goldstein, 1939) pointed to a high incidence of negative affects and "catastrophic" reactions among patients with unilateral left hemisphere damage, and indifference and euphoria in patients with right hemisphere injury (Denny-Brown, Meyer & Horenstein, 1952; Gainotti, 1972; Hécaen, Ajuriaguerra, Massonet, 1951). Hemispheric brain lesion has been significantly correlated with depression severity, patients with left-hemisphere lesions were more depressed than those with right-hemisphere or brainstem injury, and the proximity of a left-hemisphere lesion to the frontal pole was correlated with severity of depressive symptomathology (Robinson and Price, 1982; Robinson and Szetele, 1981; Lipsey, Robinson & Pearlson, 1983).

Recent studies which have tried to determine cognitive changes and laterality in affective illnesses suggest the presence of a cognitive "trait" characteristic of affective disorders. In particular, it has been found that unipolar and bipolar depressives have specific difficulties in dealing with spatial/holistic tasks (Yurgelun-Tood, et al., 1987; Robertson and Taylor, 1985). Inefficient holistic processing and decreased gestalt closure have been shown to persist in euthymic bipolar patients (Sapin, et al., 1987), and to be present in those subjects (well-offsprings of bipolar patients) who are at risk of developing a bipolar disorder (Sapin, et al., 1988).

The purpose of this study was to investigate the question of whether or not there is a cognitive marker characterized by inefficient holistic information processing in major depression. A comparison of adolescents' response pattern on specific visual tasks during acute and improved depressive state was conducted. The visual tasks administered have been demonstrated to be more reliable in activating right hemisphere functioning, and to require a holistic information approach.

METHOD

Subjects

A total of forty-three adolescents participated in this study. The experimental group of twenty-three subjects was obtained from the adolescent psychiatric unit of Miami Children's Hospital. The control group ($N = 20$) was gathered from local high school students. Subject participation was voluntary, confidential, and without any type of compensation. All subjects were screened for previous head trauma or neurological problems, alcohol or substance abuse, handedness, vision, intellectual functioning, and previous depressive or psychiatric history.

Participation on this study was limited to subjects with the following characteristics: 13–18 years of age; high school students, right-handed, with average range of intelligence, with normal or corrected vision, free of psychiatric history other than major depression in depressive group, and free of any medical, head trauma or neurological history.

The affective disorder research group was selected from the first twenty-three adolescents admitted to the Miami Children's Hospital Psychiatric Unit with a diagnosis of major depression who met the criterion for selection and had a score of 77 or more on the Reynolds Adolescent Depression Scale (RADS) (Reynolds, 1987). The group was formed by sixteen females and seven males. They had a mean age of 15.26 years and a mean Full IQ of 105.21 (VIQ = 104.43, PIQ = 105.56). The depressive group met the DSM-III-R (1987) diagnostic criteria for Major Depression. All clinical interviews and diagnostic classifications were made as part of the psychiatric unit's admission criteria usually consisting of a psychiatric interview, a medical examination, and intellectual evaluation based on the Wechsler Intelligence Scale for Children, Revised (WISC-R, Wechsler, 1974) or Wechsler Adult Intelligence Scale (WAIS-R, Wechsler, 1981). Table 1 summarizes the general characteristics of the sample.

The control group was selected from the first 20 subjects from a high school population who met the research criteria and had a score of 60 or less on the RADS. There were 14 females and 6 males. They had a mean age of 15.26 years and mean estimated IQ of 105.75. A completion of a brief demographic questionnaire, the RADS, a Handedness Inventory (Brigg & Nebes, 1975), the Shipley Institute of Living Scale, which measures intellectual functioning (Zachary, 1986) and a brief clinical interview based on the Structured Clinical Interview for DSM-III-R (Spitzer, Williams & Gibbson, 1987) were requirements of the control group for research inclusion.

The patients were informed of the research project by their primary physician and volunteered to participate in the study. None of the admitting or staff members were

TABLE 1
General Characteristics of the Sample

		Depressed	Control
	N	23	20
Age	$\bar{X}$	15.26	15.65
	SD	1.45	3.71
Sex	Male	6	6
	Female	17	14
I.Q.	$\bar{X}$	105.13	105.75
	SD	12.12	5.70
Reynolds	Pre $\bar{X}$	81.95	48.30
	SD	7.13	2.27
	Post	68.29	48.40
		11.54	1.98
Suicide	13	0	
Attempt	17	0	
Family	17	0	
History	17	0	
Medication	13	0	

aware of the hypotheses of this study when the diagnostic classification of the subject was performed.

Procedure

Tests were administered to both the experimental and control groups, in the same order, in one session and at two different intervals. There was an initial pretest and second posttest administration after four weeks. The pretest of the depressive group was given within the first five days following admission and the posttest four weeks later. All subjects were administered the following tests during the pretest phase: GSCT (Ekstrom, et al., 1976), LO, Form H (Benton, et al., 1983), HVOT (Hooper, 1983), and RCF, with a maximum score of 72 (Deman, 1987).

During the posttest the tests administered were GSCT, LO Form V, and HVOT. In addition, all subjects completed the RADS immediately prior to the posttest. This was done to rule out factors of time and the effect of treatment between the two administrations of the instruments.

The instruments used can be divided into two categories: (a) those used in the selection of subjects, i.e., RADS, the Handedness Inventory, Shipley Living Scale, the WISC-R or WAIS-R, and (b) those tests involving visual tasks, namely LO, RCF, HVOT, and GSCT.

RESULTS

Three comparisons of visual perceptual functioning were made between control and depressed groups in pretest, posttest, and their pre- and-posttest difference scores. As a statistical measurement, a *t*-test for independent samples was employed. Further, a correlation was carried out between depressives' level of depression and their performance in different visual tasks. Spearman's Correlation was used as a statistical measure to determine the magnitude of the relationship between these variables.

During the pretest condition and in comparison to the control group, depressives demonstrated impaired performance in all visual tasks (see Table 2). The greatest impairment was found in the GSCT ($t = -8.7269$; $df = 19$; $p < .0001$), following by LO ($t = -5.1818$; $df = 19$; $p < .0001$), RCF ($t = -3.0862$; $df = 19$; $p < .01$), and HVOT ($t = -2.0642$; $df = 19$, $p < .05$).

Four weeks after treatment, depressives continued to perform significantly worse than the control group. Their performance in GSCT remained impaired

TABLE 2
Mean Task Performance by Depressives and Controls during Pre and Posttest. Standard Deviations are shown in brackets

	Pretest			Posttest		
Test	Depressed	Control	*p*	Depressed	Control	*p*
Gestalt Completion	11.20 (2.50)	16.10 (0.71)	.0001	12.55 (2.54)	16.75 (0.78)	.0001
Hooper	25.15 (2.51)	27.95 (1.73)	.05	26.02 (2.93)	27.95 (0.64)	.01
Line Orientation	20.30 (5.49)	26.80 (0.83)	.0001	23.35 (3.97)	27.55 (0.82)	.001
Rey Figure	64.20 (6.28)	69.99 (1.65)	.01			

($t = -7.3171$; $df = 19$; $p < .0001$). They continued to display difficulty in LO ($t = 4.3939$; $df = 19$; $p < .001$), and in HVOT ($t = -3.0324$, $df = 19$, $p < .01$).

There was a nonsignificant difference between the control and the depressed groups in their difference-scores as measured by their difference between pre- and posttest scores in GSCT ($t = 1.7581$; $df = 17$; $p =$ NS) and in HVOT ($t = .3448$; $df = 17$; $p =$ NS). There was a very small significant difference in LO ($t = 2.9065$, $df = 17$, $p < .05$). These results indicate that performance on different visual tasks did not vary significantly as a result of the effect of treatment.

The analysis of the relationship between level of depression and performance on different visual tasks during pre- and posttest indicated that the only task significantly correlated with depression was that measuring GSCT ($r = -.45$; $p < .01$ during the pretest condition; $r = -.41$, $p < .02$ during posttest condition). Correlation of GSCT with family history of depression, use of antidepressant medication, and suicide attempt showed only a slight correlation with suicide attempt ($r = -.33$; $p < .06$).

According to the qualitative analysis of the RCF, it was found that during pretest, 16 of the depressed subjects and 17 subjects of the control group used a holistic approach. They began the copy in the upper left, capturing the outer contour of the figure with a continuous line and then adding the internal details. Conversely, seven depressives and three controls used a piecemeal approach, characterized by a breakdown of contour and organization, and juxtaposing details one by one without an organizing structure. During the posttest, only two of the depressed subjects used a piecemeal approach; in addition, the overall quality of the copies improved.

DISCUSSION

The findings of this research support prior results which have portrayed depressed patients with visuospatial deficiency (e.g., Cassens, 1988; Keating, 1988; Flor-Henry, 1976; Gray, et al., 1987; Rattan, et al., 1986; Fisher, et al., 1986; Newman & Silverstein, 1987). Overall, depressed adolescents performed significantly worse than nondepressed adolescents in all four measures of visuospatial functioning, during both pretest and posttest conditions. They demonstrated greatest difficulty in measures of GSCT and LO. The GSCT has been considered one of the purest spatial tasks (Sapin et al., 1987, 1988; Robertson & Taylor, 1985; Ekstrom et al., 1976) and the LO as one of the most reliable tasks in activating the right hemisphere (Deutsh et al., 1988). However, GSCT was the only measure to be significantly correlated with the level of depression. Thus, this suggests that a decrease in gestalt and holistic processing skills could be the result of information-processing anomalies in affective illness.

Recent investigations of the regional brain functioning in depression indicate that differences in hemispheric metabolic activity between normals and depressives depends on the task involved which, in turn, can implicate several inter-and/or intrahemispheric regions (Wexler, 1988). Research on task-dependent EEG asymmetry in depressed and nondepressed subjects has demonstrated the depressives showed opposite patterns of EEG asymmetries in the parietal and frontal region while normals displayed similar patterns; in particular, depressed subjects had greater relative right-sided frontal activation which, in turn, was associated with a right parietal inhibition. This posterior right-sided inhibition resulting from the frontal lobe activation has been suggested as a causative factor of the impaired performance shown by depressed patients on cognitive tasks mediated by the right hemisphere (Davidson, Mednick & Moss, 1987; Davidson et al., 1985, 1987).

Affective illnesses have mostly been associated with right hemisphere dysfunction not only in depressed patients, but also in those patients who have damage to or seizure in the right hemisphere and who manifest depressive or manic-depressive symptoms (Flor-Henry, 1983). Depression directly affects neuropsychological testing; however, there is not an unique neuropsychological profile characteristic of depressive disorders; neuropsychological impairment increases from major depression, to mania to schizophrenia, with a minimal right hemisphere dysfunction in unipolar depression, a more extensive right and left-frontal-temporal in bipolar disorders, and maximal bilateral dysfunction in schizophrenia (Flor-Henry, 1983; Kushnir, Gordon & Heifetz, 1980; Gray et al., 1987; Gray et al., 1987; Rattan, Gray & Dean, 1986; Newman & Sweet, 1986; Fisher, Sweet & Pfaelzer-Smith, 1986; Keating, 1988; Maj, 1986; Cassens, 1988). Severity of depression positively correlates with degree of neuropsychological impairment. In general, with increased severity of depression there is a systematic declining performance on auditory attention, visual and verbal memory, abstraction and conceptual thinking, and visuospatial functions (Cassens, 1988; Blackburn, 1975; Rush et al., 1983; Newman, 1985; Newman and Silverstein, 1987; Olcese & Purish, 1986; Robertson & Taylor, 1985; Savard, Rey & Post, 1980; Henderson, 1987; Wade et al., 1988; Yurgerlun-Tood et al., 1988; Yurgelun-Tood et al., 1987; Jones, Henderson & Welch, 1988).

The variety of these results from the studies on regional brain functioning and neuropsychological assessment in depression indicates the difficulty in finding a specific deficit associated with depression, and demonstrates the difference between subgroups of depressed patients. All these, as Wexler (1988) and Flowers & Wood (1988) argue, strongly indicate the "pathophysiological hetereogeneity" of affective disorders. However, there is an overlap of brain functioning between different diagnostic groups as well as differences between the same diagnostic group; it appears that some brain dysfunction would be represented in more than one mental disorder (Wexler, 1988; Flowers & Wood, 1988).

Taking a different perspective, Kinsbourne (1988) states that based on the available evidence, cerebral dysfunction in depression could be explained as a state marker rather than a trait marker since there are fluctuations in the cerebral functioning of depressed patients as they recovered. Moreover, it has been possible to simulate aspects of depression-related cerebral dysfunction by inducing a temporary depressed mood in normal subjects. He argues that patterns of cerebral dysfunction in depression cannot be considered specific to major affective disorders and nor can they provide any indication of what causes a major affective disorder.

Overall, the findings of this research are consistent with the observation in the neuropsychology literature of a selective deficit on visuospatial tasks assumed to be mediated by the right hemisphere (e.g., Flor-Henry, 1983). These results could be explained by recent findings of regional brain functioning in depression, which have found that depressed subjects have greater relative right sided frontal activation as compared to normals, and this right-posterior inhibition has been considered to be the immediate cause of the performance deficit observed in depressives on cognitive tasks mediated by the right hemisphere (Davidson, 1988).

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