Update on Cognition

Cognitive Impairments in Major Depression and Bipolar Disorders

by Philip D. Harvey, PhD

This regular column is written to provide readers with the latest updates on the measurement and treatment of cognitive and functional deficits in psychiatric disorders.

It has long been appreciated that episodes of major depression are associated with cognitive changes, as are periods of mixed or euphoric mania. It has also been understood that affective disorders are associated with functional disability, including decrements in both occupational and social functioning. However, in contrast to research on schizophrenia, there has been considerably less research on the connection between cognitive and functional disability. Also, given the episodic nature of affective disorders, it is important to understand the course of cognitive impairments in both major depression and bipolar disorder and to know whether cognitive impairments are persistent into euthymic states and, if so, whether the signature and severity of impairments change along with partial remission of affective symptoms.

SIGNATURE OF IMPAIRMENTS

While both depression and mania have elements of cognitive impairment as components of their diagnostic criteria, such as difficulty concentrating in major depression and behavioral evidence of distractibility in mania, there are multiple other cognitive impairments seen in both of these conditions. In fact, performance on many neuropsychological tests is impaired and some studies have found that the profile, although not necessarily the severity, of impairments is quite similar to that seen in schizophrenia.[1]

One feature of cognitive performance in depression as compared to other conditions is a bias toward processing of emotional valence in stimulus materials. For instance, research has found that patients with major depression have a difficult time avoiding processing of the emotional connotation of verbal information.[2] Interestingly, the response biases seen are not those of avoiding positive information, but rather of focusing to a maladaptive extent on negatively toned information. Such a response bias may in fact be a risk factor for depression, because several studies have found that relatives of people with depression and college students with sub-clinical signs of depression also manifest this processing bias.[3]

SEVERITY OF IMPAIRMENTS

While some research has suggested that patients with major

depression and bipolar disorder are somewhat less impaired in their performance than people with schizophrenia, other studies have found little difference in performance. In the case of major depression, the presence of psychotic symptoms has been associated with more severe impairments,[5] while in bipolar disorder, even cases with little current symptomatology are sometimes found to be as impaired as patients with schizophrenia.[6] Longitudinal data on patients with manic episodes have suggested that some features of cognitive impairment, such as excessive susceptibility to distracting information, improves with the remission of symptoms.[7]

SPECIAL FEATURES OF AFFECTIVE DISORDERS RELEVANT TO COGNITIVE FUNCTIONING

Treatment-resistant depression. One of the recent developments in the understanding of affective disorder has been the realization that there are some important potential subtypes of major depression. For example, one of the important subgroups of people with major depression is the fairly substantial group who fail to respond to pharmacological treatments. This condition, referred to as treatment-resistant depression (TRD), has been defined with several different sets of criteria all focusing on the fact that these patients often experience persistent depression for years on end. Persistent depression has been associated with cortical atrophy, which is more extreme in cases with more profound symptoms. Obvious cortical atrophy may have substantial cognitive implications, but surprisingly little research has ever been conducted on the cognitive characteristics of TRD. This is an area of major importance.

An additional issue associated with TRD is the level of impairment in functional status that is found in this group. Increased morbidity, in areas of occupational and social dysfunctions, is often found in this group. At the same time, there is remarkably little research on cognitive impairments in this group. It is unclear whether depressed mood or cognitive deficits are the factors that are associated with the increased morbidity in this subgroup. Since cognitive deficits appear more substantial during episodes of depression than during the periods of relative euthymia in treatment-responsive patients, it would be predicted that patients with TRD would manifest substantial cognitive impairments.

Vascular depression. Substantial recent research has also examined late-life onset of depressive syndromes in individuals with definite or suspected evidence of vascular changes. This syndrome, referred to as vascular depression, may be responsible for many of the cases of depression that appear in individuals who were never depressed in their younger years.

Vascular changes are well known to produce cognitive changes on their own. For instance, in severe cases of vascular changes vascular dementia is associated with cognitive impairments with a profile and severity that resembles degenerative conditions such as Alzheimer's disease. Thus, much like TRD, there are multiple potential origins of cognitive impairments: those associated with depression and those directly associated with neural damage, which is associated with vascular changes.

Studies of cognition comparing vascular depression and recurrent depression in late life have suggested

Given the relative lack of information about cognition in affective disorders, compared to schizophrenia, there are several open questions that will be the focus of research attention:

- Are TRD and bipolar depression similar in cognitive characteristics?
- Is cognitive impairment the origin of disability in affective disorders?
- Are the functional correlates of cognitive impairment the same in affective disorders?

a difference in the signature of impairments. In contrast to the prominent deficits in episodic memory seen in recurrent depression, patients with late-onset vascular depression showed a profile of impairment with prominent attention and executive functioning deficits. This is also a profile that has been reported in frontostriatal conditions such as Parkinson's disease, which is also marked by depression in many cases.

Bipolar depression. Recent interest in bipolar depression has been spurred by two recent developments. The first is the fact that atypical antipsychotic medications have been approved for the treatment of bipolar depression. The second is the concurrent realization that bipolar patients who recover from manic or mixed episodes still manifest substantial remaining depressive symptoms. These symptoms are associated with increased risk for suicide and reduced subjective quality of life. Thus, the presumed episodic nature of bipolar disorder may be influenced by the persistence of depressive symptoms during periods of relative remission from manic-type symptoms.

Since patients with particularly persistent bipolar depression are also the patients who show the lowest rates of functional recovery from mixed or manic episodes, it is also likely that these patients are also showing persistent cognitive changes. Again, this is an area where there is no substantial research base. It is not clear if the cognitive impairment profile and severity in bipolar depression is similar to treatment-responsive or treatment-resistant depression.

Other open questions. Given the relative lack of information about cognition in affective disorders, compared to schizophrenia, there are several open questions that will be the focus of research attention.

Are TRD and bipolar depression similar in cognitive characteristics? Since both TRD and bipolar depression are syndromes of persistent depression (in individuals who do and do not have manic episodes) are their cognitive characteristics similar as well?

Is cognitive impairment the origin of disability in affective disorders? Since studies of recovery from bipolar disorder have often not assessed cognition during the acute phases, it is difficult to determine if persistent disability in some cases is associated with persistent cognitive deficits?

Are the functional correlates of cognitive impairment the same in affective disorders? There has been little to no research on the ability to perform functional skills in affective disorders. Since deficits in skills competence is strongly associated with cognitive deficit in schizophrenia, the same relationships might be seen in affective disorders.

Recent increases in the sophistication and functional relevance of studies of cognition in schizophrenia have led to several initiatives aimed at the treatment of cognitive impairments (such as the MATRICS initiative described in the last column [October issue of *Psychiatry 2006*]). Research and clinical treatment of affective disorders will also be improved through the use of some of these innovations as well.

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