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REVIEW

Depression and Cognition

Yong Tae Kwak,[1] YoungSoon Yang,[2] Min-Seong Koo[3]

[1]Department of Neurology, Hyoja Geriatric Hospital, Yongin, Korea
[2]Department of Neurology, Seoul Veterans Hospital, Seoul, Korea
[3]Department of Psychiatry, College of Medicine, Catholic Kwandong University, Gangneung, Korea

Depression is a relatively common agonizing psychiatric disorder that affects the way we feel and think about ourselves and the world around us. Cognitive theories of depression have long posited that various cognitive biases are involved in the development and recurrence of depression. However, the current cognitive theory of depression has been reformulated and expanded from the previous cognitive model of depression based on the results from pharmacological, neuroimaging and neurocognitive studies. This review summarizes the evidence for cognitive dysfunctions in depression and the related pharmacological, neuroanatomical and genetic aspects which aim to integrate our knowledge about the cognitive aspects of depression and its treatment. The newly formulated cognitive theory of depression provides directions for future investigation to identify people at risk, to minimize recurrence, and to maximize long-term beneficial outcomes for those suffering from depression.

Key Words depression, cognitive theory, cognitive dysfunction.

INTRODUCTION

Depression not only changes the way we feel, it also changes how we perceive ourselves and the world around us. Negative views about the self, the world, and the future (Beck's triad, Fig. 1), as well as uncontrollable recurrent negative thoughts, are agonizing symptoms of depression. Although cognitive disturbance is recognized as an "accompanying" finding of major depressive disorder (MDD) in the current diagnostic criteria [diagnostic and statistical manual of mental disorders, fifth edition (DSM-V)], cognition is regarded as a key component of depression in the cognitive theory of depression.

According to the cognitive theory of depression, people's attitudes, thoughts, inferences, interpretations, and the way in which they attend to and recall events can trigger depression development and recurrence. Indeed, the cognitive theory em-

braces vulnerability-stress hypotheses which proposed that the development of depression is due to the interaction of a cognitive vulnerability (e.g., certain cognitions or ways of thought processing information) and a precipitating stressor (e.g., a negative event or some social and environmental factor). Thus, this is a kind of continuum approach which suggests that depression is not qualitatively different from normal mood but quantitatively different from normal mood. According to this theory, one of the most effective interventions for depression is modifying biased cognitive pattern and it claims that reconstructing biased interpretations and dysfunctional automatic thought will result in improvement of other symptoms of the disorder, including sustained negative mood and lack of interest.[1]

However, the modern cognitive theory of depression has been reconstituted and expanded from Beck's cognitive model of depression based on the results from recent pharmacological, neuroimaging, neurocognitive and genetic studies. This integrated approach proposes that dysfunction of the monoaminergic neurotransmitter systems leads to alteration in the bottom-up processing of emotional stimuli, which results in negative perceptions during depression. Moreover, the result-
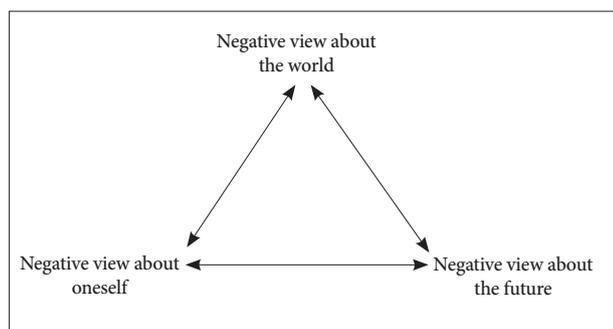
Fig. 1. Three negative schemas, cognition about the self, the world, and the future.

ing negative biases and schemata themselves also can generate top-down processing manifested as negative expectations which sustain negative schemata.[2]

In this paper, we integrate more recent studies assessing cognition and depression, and discuss the limitations of work in this field to date. From the previous reports, we review the characteristics of depression that underscore its several key cognitive features. Finally, we briefly discuss the implications of this theory for the treatment of depression and future integrative investigations on the psychological and neuro-biological aspects of this disorder.

Clinical aspects

MDD is characterized by a set of emotional, behavioral and cognitive symptoms, including psychomotor agitation (or retardation), extreme feelings of guilt (or worthlessness), insomnia (or hypersomnia), fatigue, marked weight loss, decreased appetite, concentration difficulties, and suicidal ideation. Although all these symptoms of MDD are important, depression is basically a disorder of emotional dysregulation and sustained loss of pleasure according to the current diagnostic concept. In DSM-V, application of these core criterion symptoms to the diagnosis of MDD has not changed from that in DSM-IV.

Depression is a highly recurrent disorder. More than 75% of patients with depression have more than one outbreak of depression, often relapsing within two years of remission from depression.[3] Such a high recurrence rate suggests that there are specific factors increasing the repeated recurrence of this disorder. Cognitive biases in the processing of emotional information may be the important factors.

Cognitive theory of depression

In 1976, Beck proposed that existing memory representations (or schemas), lead individuals to filter stimuli from the environment such that their attention is directed toward information that is congruent with their schemas.[1] This theory

views development and relapse of depression as a result of the persistent, self-reinforcing, maladaptive negative schemata, dysfunctional attitudes and attributional styles. Negative expectations lead to the emergence of depressive thinking processes such as negative emotional biases, negative automatic thoughts or rumination, which consequently contribute to abnormal "hot" cognitive processing in a top-down manner. Accordingly, Beck and other researchers proposed interventions to reconstruct patterns of maladaptive thoughts and behaviors, and they claimed that these changes would improve other symptoms of depression.

The current cognitive theory of depression suggests that the negative schemata are not the direct result of negative early experiences, but instead are triggered by dysfunctional affective processing biases of multiple origins. The most important conceptualized origin of biases may be alterations in monoamine transmission. Although at first glance, this difference may appear negligible, its implications are substantial.

In contrast to the earlier pure psychological theory, the modern cognitive theory of depression embraces recent pharmacological and neurocognitive achievements. This integrated approach postulates that dysfunction of the monoaminergic neurotransmitter systems, which might be related to either environmental or genetic factors or more likely to a combination of both, altered the bottom-up processing of emotional stimuli and this resulted in negative perceptions during depression. Consequent negative biases and schemata resulting from the decreased monoaminergic modulation in neural circuits during emotional processing can be influenced by manipulation of monoaminergic neurotransmission.[2,4]

These dysfunctional negative schemata also can generate top-down biases and these manifest as negative expectations which again sustain and enforce negative schemata.[2] Selective serotonin reuptake inhibitors can decrease symptoms by influencing bottom-up negative biases; however, this strategy may only be fully successful if correction of their dysfunctional cognitive processes is subsequently reformulaed their top-down biases. This is also supported by the fact that pharmaco-cognitive combination therapy is significantly more effective compared to either method on its own.[5] In particular, the cognitive theory approach emphasizes the critical role of negative affective biases in the development and treatment of depression; moreover, it provides a theoretical background in which the traditional purely 'psychological' and the recently developed 'neurochemical' model of depression might be reconciled.

Hot and cold cognitive deficits

Although the patients with depression demonstrate diverse cognitive dysfunctions, there are two distinct cognitive dys-

function patterns correlating mood and emotional symptoms of depression and dysphoria. To understand the various subtle cognitive alterations in depression, differentiating affect-independent (or cold) and affect-laden (or hot) cognitive functions is necessary. Cold cognitive dysfunctions in patients with depression are general deficits in cognitive functioning such as difficulties, distractibility, impairments in memory[6] and difficulties disengaging from negative images.[7] There are hot cognitive dysfunctions in depressed patients; despite these cold cognitive dysfunctions, they exhibit easy concentration on negative self-focused thoughts, and they show enhanced recall of mood-congruent (i.e., negatively valenced) events.[8]

"Cold" cognition refers to information processing independent of emotional status and can be assessed with commonly used formal neurocognitive tests where the stimulus is emotionally neutral and the result of the test is not generally dependent on motivation.[9] On the contrary, "hot" cognition indicates information processing influenced by emotional status and can be recognized during a conversation or in a test related to stimuli carrying emotional valence. In patients with depression, cognitive dysfunctions congruent with mood are reported in several cognitive domains and other domains abnormalities related to cognitive processing of reward and punishment have also been reported. In various perception, memory, attention and working memory tests related to emotional processing, patients with depression give more negatively biased answers. Furthermore, altered performance in reward- and punishment processing was identified in patients with depression, and these findings suggested an enhanced sensitivity towards negative feedback and a reduced sensitivity towards positive feedback, and decreased learning capability related to rewarding cues.[2,6,9]

However, "cold" cognitive deficits observed in patients with depression can also be influenced by alterations in "hot" cognitive processing, i.e., emotion-independent cognitive tasks frequently become emotion-laden in patients with depression, which is especially observed in feedback-based tasks. In response to task failure, catastrophic reaction was frequently observed in patients with depression, i.e., they show a higher error rate in the next trial after one mistake.[2,6] These findings suggest that neurocognitive dysfunctions in patients with depression play a fundamental role in the manifestation of other depressive symptoms.

Trait and state cognitive deficits in depression

Certain cognitive deficits in patients with depression may exclusively occur during depressive episodes and are also observed between episodes or even prior to the outbreak of depression. By identifying trait and state cognitive changes, it would be possible to explore these cognitive changes and dysfunctions which are present even preceding the episode of depression. These can also be found in first-degree non-affected relatives and could therefore be considered as trait-like vulnerability markers. Furthermore, it is important to explore and assess these residual cognitive symptoms which are present after the recovery of depressive episodes, since they can profoundly and persistently affect the quality of life and function of patients with depression.

Cognitive deficit in patients with depression

Executive function deficit

Executive functions are a set of higher-level processes–including attentional control, inhibitory control, working memory, cognitive flexibility, reasoning, problem solving, and planning–that are necessary for the control and coordination with other cognitive abilities and behaviors. These selecting and successful monitoring of behaviors facilitate the attainment of chosen goals.

There is mixed evidence for executive function deficits associated with MDD. Although many studies have reported significant deficits on many neuropsychological tests of executive function, other studies have reported no significant deficit in patients with MDD compared to healthy control participants. However, several recent reviews have found partial support for deficits across multiple domains of executive function, including working memory, shifting, inhibition, planning, and verbal fluency.[10-12] These deficits were also present in unmedicated MDD patients.[13] Moreover, these executive dysfunctions were also present in remitted cases despite improvement of depression,[14] particularly in older adults.[15]

Consistent with these neuropsychological findings, functional imaging and human lesion studies have reported dysfunction of the dorsal and lateral prefrontal cortex in depressed patients performing executive tasks, although these structures interact with subcortical structures and posterior cortical regions.[16]

Interestingly, the activation of these structures differs according to the cognitive tests. For example, tests of forward planning[17] or verbal fluency[18] showed attenuated prefrontal activation in the MDD group compared to healthy controls. However, working memory task,[19] mental arithmetic task,[20] and the Stroop task[21] showed greater prefrontal activation in MDD, wherein there were no differences in performance between patients and healthy controls. Although the reason for these inconsistencies may not be clear, exaggerated activation may suggest reduced cortical efficiency; i.e., patients with depression may require greater frontal lobe activation to main-

tain a comparable level of task performance to that in healthy controls.

Memory

Various memory function deficits, including a virtual reality spatial navigation task[22] or paragraph recall (remembering the details of a complex story after a 10-min delay), have been reported in patients with depression.[23] Moreover, memory impairment is highly predictive of functional outcome and correlates with indices of illness chronicity.[24]

This pronounced memory deficit may be due to hippocampal dysfunction. Hippocampal function is impaired in patients with MDD during memory encoding tasks,[25] and reduced hippocampal volume is arguably the most robust neuropathological finding reported in MDD, supported by meta-analyses of MRI data[26] as well as postmortem evidence.[27]

Affective processing bias

The symptoms of depression suggest a processing bias toward negative aspects of the environment. For example, more enhanced recall of negative compared to positive material is one of the most consistent findings in depression studies.[8,28] Patients with depression are more likely to recall negative autobiographical memories, and when they recall positive memories, they are lacking in detail, i.e., characteristically overgeneral.[29] In contrast, healthy participants typically show a bias for positive material. These findings are more consistently reported in the explicit memory test than in the implicit memory test in patients with depression.

The task of recognizing emotional facial expression or the task that presents emotional words or pictures is a widely used test for affection processing bias in neurocognitive and functional imaging studies. The patients with depression are impaired in recognizing happy facial expressions, whereas manic patients are impaired in recognizing negative (including sad) facial expressions.[30] The affective go/no-go test is also used to identify these biases and this test requires the processing of affect in the context of an inhibitory control task. In this test, depressed patients responded more rapidly to sad versus happy word targets, whereas manic patients displayed the opposite bias, responding faster to happy words.[31]

Feedback sensitivity

The patients with depression tend to ruminate over failures and criticism. Patients with depression also have an exaggerated response to negative feedback during the neuropsychological test of confrontation. An early study using two tests of working memory and forward planning reported that if patients with MDD responded incorrectly on a given trial, they were disproportionately likely to fail the subsequent trial.[17] This exaggerated response to previous failure occurred across both tasks and could influence the cognitive ability on any tasks that deliver performance-contingent feedback. Moreover, this feedback sensitivity appeared specific to depression because it was not seen in other neuropsychiatric conditions that showed overall task impairments, such as Parkinson's disease.[32]

In addition to abnormal processing of negative feedback in depression, the anhedonic symptoms of depression, wherein the patients fail to derive enjoyment from pleasurable activities, suggest that there may also be altered processing of positively valenced information in MDD. As such, anhedonia appears to reflect both a blunting of positive reinforcement processing, as well as an inability to use negative feedback to improve task performance.

Related anatomy

Numerous imaging, postmortem, and laboratory studies showed diverse depression-related anatomy. Dorsal and lateral prefrontal cortex dysfunctions in functional imaging studies were found in depressed patients performing executive tasks. Hippocampal dysfunction is impaired during memory encoding tasks[33] and reduced hippocampal volume is the most consistently reported neuropathological finding in MDD.[27] Right orbitofrontal cortex and amygdala showed abnormally increased neural responses to sad targets and negative emotional faces.[34] The amygdala is extensively interconnected with the multiple regions within the prefrontal cortex, and these interactions may allow top-down control of emotional behavior.

Biological factors related to cognition

Biased cognitive processes may interact with genetic and neurobiological vulnerability factors.[35] For example, variations in the serotonin transporter gene (5-HTTLPR) are known to be vulnerability factors for depression through their effects on social cognition.[36] This gene-by-environment view of depression showed a recent integrative cognitive hypothesis which explains depression as the result of interplay among genes, neuroendocrine, and stress in relation to various cognitive biases.[37]

Cognition and depression in Alzheimer's disease

Although Alzheimer's disease (AD) is a neurodegenerative disease characterized by impairment in various cognitive functions, depression is one of the most frequent accompanying psychiatric symptoms of AD, with 30% to 50% prevalence.[38] The cognitive aspects of depression in patients with AD have been less studied compared to those of early-onset depression. Cognition is primarily and persistently affected during disease progression in AD, and according to the cognitive theory of

cal reconsolidation. This view is consistent with cognitive theory of depression which emphasizes the role of negative biases in information processing in the development and relapse of depression and the importance of correcting such biases in successful treatment of this disorder.[1]

CONCLUSION

Depression is associated with cognition, and several domains of cognition (including hot cognition) are primarily affected. These cognitive dysfunctions may have a critical role in the development of depression and response to treatment. The modern cognitive theory of depression has been reformulated and expanded from the original cognitive model of depression based on the results from recent depression studies. This integrated approach had a profound effect on understanding the pathophysiology and treatment of depression.

According to the modern cognition theory of depression, future studies will benefit from integrative research in cognitive science which embraces the genetic, neural, cognitive, and affective aspects of depression.

Conflicts of Interest

The authors have no financial conflicts of interest.

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