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• Forum •

Subthreshold depression

Are subsyndromal symptomatic depression and major depressive disorder distinct disorders?

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Depressive conditions that do not meet full symptomatic or duration criteria for a major depressive disorder (MDD) are of considerable interest to both clinicians and researchers.[1-4] The fourth edition of the American Psychiatric Association *Diagnostic and Statistical Manual of Mental Disorders* (DSM-IV) provides descriptions of several types of subthreshold depressive states including dysthymia, minor depression and recurrent brief depression; but many individuals with subthreshold depression and associated impaired functioning do not meet DSM-IV diagnostic criteria for any of these disorders.[3] To cover these cases Judd and colleagues[4] proposed the concept of 'Subsyndromal Symptomatic Depression' (SSD) for individuals without depressed affect or anhedonia who have two or more (but less than five) of the other seven symptoms of depression that have been present for most of the time for at least two weeks and that are associated with impaired social functioning.[3,4] The appropriate diagnosis and treatment of individuals with this type of subthreshold depression will require a better understanding of the relationship between SSD and MDD. Are they independent disorders or is SSD a transitional state on the road to MDD?

SSD is a relatively common condition. Based on the Epidemiological Catchment Area study in the United States, Judd and colleagues estimated a 12-month prevalence of SSD of 8.4% in the general population; the prevalence in women was double that in men and was particularly high in women who were unmarried and unemployed.[5] A study in Australia reported a 12.9% prevalence in the general population and found that the quality of life for persons with SDD was intermediate, between that for persons without any depressive symptoms and that for persons who met criteria for MDD.[6] A survey of people aged 60 and above in Singapore found that SSD was more common in individuals with a lower socioeconomic status and was often associated with cognitive impairment, anxiety, poor physical health, and poor social functioning.[7]

The clinical presentation of SSD is similar to that for other types of depressive disorders.[5] Common symptoms include sleep disturbances (44.7%), prolonged fatigue (42.1%), repetitive thoughts of death (31%), and difficulty concentrating (22.7%). Atypical symptoms such as weight gain, slowed thinking and hypersomnia are somewhat more common in individuals with SSD than in those with minor depression. Risk of suicide is lower among SSD patients than in patients with minor depression or major depressive disorder.[5]

In China, Li and colleagues[8] report that common symptoms in SSD include hypersomnia, fatigue, difficulty concentrating, increased appetite, and slowed thinking. These symptoms are also common in physical illnesses, so many individuals with SSD seek treatment from the internal medicine departments of general hospitals, which delays the diagnosis and treatment of the SSD. Li and colleagues also compared SSD and MDD and found no differences in the reported quality of marriage and in the rates of suicide attempts.[8] However, they also reported individuals with SSD were more likely than those with MDD to be female, had a higher educational level, were more likely to seek treatment from departments of internal medicine (rather than from mental health services), and had fewer days out of role but more days in which they felt unproductive in the prior year.[8]

Research on SSD in China has also considered potential biological markers that could distinguish it from other depressive conditions. Cheng and colleagues[9] found that abnormal sympathetic skin responses are more likely to occur in SSD patients than in normal controls. Using the classification of gene expression profiles from peripheral blood leukocytes, Yi and colleagues[10] found that the gene expression profiles in SSD patients were different

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from those in healthy control subjects and from those in MDD patients; based on these findings they built a 48-gene expression signature model that could potentially serve as diagnostic biomarkers of SSD and MDD. Studies from Professor Yiru Fang's team[11,12] conclude that the etiological mechanism of SSD involves neuroendocrine, neuroimmune, and neurotrophic factors that influence several components in the neurotransmission process including neuroreceptors, G protein, intraneuron signal transmission, gene translation, and the synthesis of proteins and neuropeptides. Their findings support the hypothesis that SSD is related to abnormalities in neuron apoptosis. They find underexpression of Bcl-12 and brain-derived neurotrophic factor (BDNF),[11,12] which are directly related to the differentiation and survival of neurons and to synaptic development.[13]

A three-year follow-up study conducted 15 years ago found that the remission rates in SSD (defined as no symptoms or only one symptom of depression) are similar to those in MDD (57% remitted in both groups).[14] Despite this parallelism, some researchers now think SSD should be considered a stand-alone condition that may or may not co-exist with MDD. Research from our team in China supports this view. Significant heterogeneity between SSD and MDD in personality traits, neurobiochemical characteristics,[15] and gene expression suggests that they do not belong to the same spectrum of disease and should therefore be treated as independent mental disorders.

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