ME/CFS is not synonymous with depression or other psychiatric illnesses. The belief by some that they are the same has caused much confusion in the past, and inappropriate treatment.

Careful attention to the timing and correlation of symptoms, and a search for those characteristics of the symptoms that help to differentiate between diagnoses may be informative, e.g., exercise will tend to ameliorate depression whereas excessive exercise tends to have an adverse effect on ME/CFS patients. Response to therapy directed at a presumed psychiatric entity may be a helpful distinguishing feature.

1. **Depression** may come independent of ME/CFS, or patients may feel sudden waves of depression, which just come and go erratically, and are not tied to any definite external context. These attacks are often a secondary consequence of a chronic illness. Since patients live in a depressing situation with severe social and activity restrictions at work, play and in relationships, it is not surprising that situational depression occurs in a subset of patients in reaction to their illness. These various forms of depression can often be distinguished by careful attention to the dynamics of their progression, their temporal relation to other symptoms, their degree of appropriateness, the effect of exercise, etc. Primary depression may cause a significant symptom overlap with ME/CFS, by resulting in fatigue, sleep disturbances and poor concentration.

A comparative study indicated a qualitative difference between the ‘depressive symptoms’ of ME/CFS and those of depression (53). ME/CFS patients scored higher on items indicating physical complaints and symptoms of fatigue and they scored less frequently for disturbed mood and self-reproach than did depressed patients (53,54). In general, fatigue is not as severe in depression as in ME/CFS. Joint and muscle pains, recurrent sore throats, tender lymph nodes, various cardiopulmonary symptoms (55), pressure headaches, prolonged post-exertional fatigue, chronic orthostatic intolerance, tachycardia, irritable bowel syndrome, bladder dysfunction, sinus and upper respiratory infections, new sensitivities to food, medications and chemicals, and atopy, new premenstrual syndrome, and sudden onset are commonly seen in ME/CFS, but not in depression. ME/CFS patients have a different immunological profile (56), and are more likely to have a down-regulation of the pituitary/adrenal axis (57). Anhedonia and self-reproach symptoms are not commonly seen in ME/CFS unless a concomitant depression is also present (58). The poor concentration found in depression is not associated with a cluster of other cognitive impairments, as is common in ME/CFS. EEG brain mapping (59,60) and levels of low molecular weight RNase L (21,26) clearly distinguish ME/CFS from depression.


2. **Somatoform Disorder**: There is some symptom overlap between somatoform disorders and ME/CFS. There are numerous objective findings in patients with myalgic encephalomyelitis/chronic fatigue syndrome, including abnormalities in brain SPECT scans and qEEG brain topography, orthostatic intolerance and dysregulation of the 2-5A synthetase/RNase L antiviral defense pathway and low molecular weight 37kDa Rnase L. These can be used to exclude somatization disorder in doubtful cases. Patients meeting the criteria of ME/CFS must be excluded from the diagnosis of Somatoform Disorder. Member countries of the World Health Organization (WHO) are obliged to adhere to the regulations of the WHO’s International Classification of Diseases (ICD) and use their ICD classification. In a letter dated January 23, 2004, Andrei I’ Hours of WHO headquarters clarified that “it is not permitted for the
same condition to be classified to more than one rubric as this would mean that the individual categories and subcategories were no longer mutually exclusive”. Thus, ME (and CFS), classified as a neurological disease in the WHO ICD, cannot also be classified as somatoform disorder, which is classified as a mental or behaviour disorder.

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