rates, and by indicators such as IQ, attention, and school and work functioning.[8-11]

Throughout the global schizophrenia literature, age at onset is consistently reported to occur approximately three to five years earlier in men than women.[12] In men age at onset peaks between ages 18-25, whereas in women this peak occurs between ages 25-35.[13] Unlike men, women appear to have an additional, smaller peak period of onset after the age of 40.[7,14] Moreover the preponderance of late-onset schizophrenia, defined as illness beginning after the age of 45, occurs in women.[15,16] However, the overall difference in age of onset appears to be accounted for by sporadic, but not familial schizophrenia – males and females with strong genetic loading have similarly early onsets.[3] Likewise, Meltzer and coworkers[17] reported a later age of onset in treatment responsive female patients, a difference not seen among non-responsive patients.

Symptom Expression and Course of Illness

Most, but not all, studies suggest that mood symptoms and specific positive symptoms (eg, paranoia, persecutory delusions, and auditory hallucinations) are common in women with schizophrenia, while negative symptoms (eg, social withdrawal, blunted affect, and amotivation) tend to be more predominant in men.[18-21] Inconsistency within these findings may relate to inadequate methodology as well as the absence of operational criteria and standardized interviews.[7] Additionally, because women tend to have more affective, cyclical, and atypical symptoms, there is less diagnostic concordance for women than men.[3]

In women with schizophrenia, symptoms tend to be relatively mild early in the course of illness. However as women age, these symptoms are apt to become more severe, whereas in men they tend to diminish.[22] Additionally, women with late-life schizophrenia are inclined to develop a more severe form of the illness than their male counterparts.[2,23]

Irrespective of sex differences in symptomatology, women appear to have a more favorable course of illness and better psychosocial outcome than men, manifested by lower rehospitalization rates and shorter lengths of stay, longer time to relapse, and better social adjustment and rehabilitative capacity.[1,24-26] Women tend to receive better care, even when there are no differences in symptom severity or psychosocial factors; they attend outpatient appointments more frequently and receive more psychological, psychotherapeutic, and social rehabilitative care.[1] Although women with schizophrenia have lower suicide and overall mortality rates than their male counterparts,[27] female patients may experience more medical comorbidity.[28] The poorer social course of schizophrenia in men appears to relate to 1) their lower level of premorbid function; 2) the impact of their earlier age at onset on social development; and 3) their greater tendency to engage in socially adverse illness behavior (self neglect, treatment noncompliance, and substance abuse).[2,25] Additionally, families of male patients tend to be more critical, and males are more susceptible to relapse as a consequence of a "high expressed emotion" family environment.[29]

Neuroanatomy and Neuropsychological Function

Although less consistently reported, some studies indicate that women with schizophrenia have fewer and less severe structural brain abnormalities and cognitive deficits than men with the illness.[30,31] More specifically, males (but not females) have shown enlarged ventricles,[31,32] decreased temporal lobe volumes,[33] decreased volume in language-associated regions,[34] and more asymmetries.[35-37] While fewer studies show no difference or greater structural brain abnormality in women,[38] there may still be differential patterns of neurological impairment by gender.[39,40]

Studies of sex differences in neuropsychological performance in schizophrenia show conflicting results, possibly due to methodological limitations such as sampling bias and lack of adequate controls.[41] Perhaps the most consistent finding is better verbal performance in women than men,[42-45] though this difference may be mediated by sex differences in normal laterality of neuropsychological functioning.[46] Several studies demonstrate either no difference[47-49] or worse performance in females than males,[50-54] although some of the women in these samples were described as more impaired due to early onset or overall poorer outcome than average.

Antipsychotic Treatment Response

Many, though not all, studies suggest that, irrespective of body weight, pre-menopausal women with schizophrenia require lower doses and achieve higher