

Abstract

Background: Neurological soft-signs (NSS) refer to subtle neurological abnormalities affecting motor coordination, sensory integration and disinhibition, and has been proposed to be putative markers of schizophrenia. There is abundant evidence showing disease association and familial association between NSS and schizophrenia. In addition, recent literature showed high levels of NSS to be associated with treatment-resistance in schizophrenia, but these studies were limited by short follow-up duration, loose definition of poor treatment response, and absence of a proper comparison group. Also, the temporal stability of NSS, which is an important feature of endophenotypic marker, remains unclear. The main objectives of this study were to examine whether NSS are associated with treatment response in schizophrenia, and whether NSS are temporally stable. We also examined the different patterns of longitudinal NSS progression in the two groups of patients.

Methods: This longitudinal study recruited and followed up first-episode schizophrenia patients for more than five years after service entry, and compared 31 patients with good treatment response (“good-responders”) with 28 treatment-resistant patients (“poor-responders”). All participants were assessed at four time-points (baseline, sixth-month, 12th-month and fifth-year) for their NSS, clinical symptoms, and neurocognitive functions. The trajectory of NSS progression between the two groups were compared using mixed model ANOVAs.

Results: The “poor-responders” had, in general, higher levels of NSS than the “good-responders”. The two schizophrenia groups with different treatment response showed different patterns of change in NSS over the five years of follow-up. These findings remained significant even when the effects of IQ and education were controlled for.

Conclusions: Our study has a refined design in terms of long follow-up duration, multiple assessment time-points, and stringent definition of poor treatment response in schizophrenia. Our findings apparently support the notion that high levels of NSS are putative markers of treatment-resistance in schizophrenia. However, NSS fluctuate along the disease course, and do not show temporal stability. Taken together our findings with previous evidence, NSS appear to reflect subtle neurobiological abnormalities in schizophrenia, which are believed to be more severe in treatment-resistant patients. However, the small sample size and practice effect of patients are limitations of this study.

Keywords: Schizophrenia; Neurological soft-signs; Treatment response; Treatment-resistant schizophrenia