

# Childhood adversities and Psychosis

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## Valorisation

The present thesis suggests that: (a) psychotic patients with childhood adversity might show worse clinical outcomes (e.g., more severe symptoms; cognitive impairments; HPA-axis dysregulation; higher sensitivity to stress) than those who were not exposed; (b) the impact of childhood adversity on psychosis seems also influenced by factors such as recent life events, HPA-axis dysregulation, cognitive functioning.

From a clinical point of view these findings might have implications in terms of assessment and treatment. The differences observed between patients with psychosis with early adversity and those without in terms of clinical outcomes may enrich the debate on the clinical validity and reliability of current diagnostic systems (Cosci and Fava 2013; First et al 2018; Maj 2018).

According to the customary clinical taxonomy in psychiatry, within the psychotic spectrum disorder, patients might be classified across different diagnostic categories resulting from the presence of a certain number of symptoms (APA 2013; Heckers et al 2013; Van Os 2015). However, it should be noted that, the clinical assessment of psychotic patients exclusively reliance on diagnostic criteria might impoverishes the clinical process given that: (a) patients with and without childhood adversities, even though clinically different, might be classified under the same diagnostic category; (b) although psychotic patients with early adversity due to their poor outcome might be more resistant to treatment (Hassan and De Luca 2015; van Nierop et al 2016), any variables that might demarcate prognostic and therapeutic differences, as life events and/or severity of illness, are not taken into account.

This underscores the need for a more complete assessment of patients with psychotic disorder, which expands the narrow range of information based on the customary nosography by including the evaluation of childhood adversities and clinical outcomes related to them (e.g. pattern of symptom; severity of symptoms). The clinimetric approach (Feinstein 1982; Fava et al 2012ab) and the stratified medicine perspective (Kapur et al 2012; van Winkel 2015) have been proposed as strategies to improve the clinical assessment beyond the current traditional nosography approach.

Clinimetrics' is the term introduced by Feinstein in the early 1980s to indicate a domain concerned with the measurement of clinical issues that do not find room in customary clinical taxonomy. Such issues include types, severity and sequence of symptoms, rate of progression in illness (staging); severity of comorbidity, life events, and many other aspects of daily life, such as well-being and distress (Feinstein 1982; Fava et al 2012ab).

The stratified medicine perspective presupposes to focus on clinically meaningful differences between clinical populations through the identification of valid markers (Kapur et al 2012). This approach allows to target specific subgroups of patients in terms of personalised

prevention, treatment and lifestyle interventions (van Winkel 2015). According to previous studies (van Winkel 2015) this thesis suggested that childhood adversities might be a suitable environmental marker to distinguish clinical significant subgroups within patients with psychotic disorder.

In addition, the present findings suggest that the cognitive functioning and the sensitivity to stress might act as a protective buffer against the impact of childhood adversity on the persistence and severity of psychotic symptoms. Thus, treatment aimed to improve neurocognitive and mentalizing abilities (Bartels-Velthuis et al 2011; Weijers et al 2016) and/or reducing sensitivity to stress in daily life (Myin-Germeys and van Os 2007; Jaya et al 2016) could be considered in psychotic patients who were exposed to childhood adversities.

Furthermore, this thesis underlines that the impact of early adversity on the risk of onset or persistence of psychosis might be amplified by the exposure to adulthood stressful events. This provides additional awareness on the detrimental effects of social disadvantages on mental health (Morgan et al 2010; Morgan et al 2014) which may increase efforts for primary prevention.

From the scientific perspective, this thesis adds to the body of the literature stressing the importance of childhood adverse experiences in the development of psychosis filling a gap (Bentall et al 2014; Ajnakina et al 2016). Indeed, most of the existing studies aimed at identifying the pathway between childhood adversity and psychosis focused on diagnostic categories rather than on symptoms dimensions (van Os et al. 1999; Bentall et al 2014; Ajnakina et al 2016) and studied childhood life events as a whole rather than different kinds of early adversity which are known to potentially increase risk for different psychotic symptoms (Bentall et al 2014).

Finally, the present findings suggest that sex differences and duration of illness should be taken into account in the investigation of the pathways linking early adversity to psychosis. These pathways could be different for males and females as well as for first onset psychosis and persistent psychosis. Future research should address these topics.