EDITORIAL: VULNERABILITY TO PSYCHOSOCIAL DISABILITY IN PSYCHOSIS

Running Head: Vulnerability to Psychosocial Disability in Psychosis

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Abstract

Psychosocial disability affects a number of individuals with psychosis and often begins years before the formal onset of disorder. This suggests that for many, their psychosocial disability is enduring, and targeted interventions are therefore needed earlier in their developmental trajectories to ensure that psychosocial disability does not become entrenched. Poor psychosocial functioning also affects individuals with a range of different emerging mental health problems, putting these young people at risk of long-term social marginalisation and economic disadvantage; all of which are known risk factors for the development of psychosis. Identification of the markers of poor psychosocial functioning will help to inform effective treatments.

This editorial will discern the early trajectories and markers of poor psychosocial outcome in psychosis, and highlight which individuals are most at risk of having a poor outcome. The editorial will also discuss whether early interventions are currently being targeted appropriately and will propose how intervention and preventative strategies can be implemented, to restore psychosocial trajectories in a way that enables young people to maximize their life chances.

Key words: Psychosocial functioning; Outcome; Cognition; Early Intervention and Prevention.

Introduction

Psychosocial disability is a term which describes social and economic challenges or consequences which can be associated with one's mental health condition, affecting a person's ability to participate fully in society, such as being involved in work or education, engaging in interpersonal relations and social activities (United Nation Convention on the Rights of Persons with Disabilities, 2016). Psychosis is the most common cause of psychosocial disability world-wide (Hafner & an der Heiden, 1999). In the UK, an estimated cost of £3.4 billion per annum is attributed to unemployment, absence from work and premature death in individuals with psychosis (Mangalore & Knapp, 2007). Psychosocial disability, or poor functioning, emerges long before the formal onset of psychosis, but peaks at illness onset and plateaus thereafter, suggesting that disability is a longstanding trait rather than direct sequela of the symptoms used to classify the disorder – hallucinations, delusions and thought disorders (Agerbo *et al*., 2004). In contrast, these symptoms peak at the onset of illness, but typically resolve - often with the initiation of anti-psychotic medication. However, it is now widely acknowledged that anti-psychotic medication has little positive impact on psychosocial disability (McGorry *et al*., 2008), highlighting that symptoms and functioning are not causally related and indicating the need for alternative therapeutic approaches.

The first episode of psychosis (FEP) often occurs in adolescence; this is a critical time for the young person's identity formation, development of social networks, and the beginnings of a vocational career; thus, disruption to an individual's social relationships and academic or work performance at this time can have a profound negative impact on their social and interpersonal trajectories (Hafner & an der Heiden, 1999; McGorry et al., 2008). Hafner and colleagues (1999) suggested that the number of social developmental milestones achieved prior to the onset of illness would strongly influence and perhaps place a limit on the long term psychosocial outcomes. Indeed, longitudinal studies have shown that psychosocial disability at

illness onset is strongly predictive of disability many years later (Addington & Addington, 2005; Alvarez-Jimenez *et al*., 2012; Tandberg *et al*., 2012), and those with an earlier onset of illness are likely to have a poorer psychosocial outcome (Hafner & an der Heiden, 1999). The logic of this is that interventions which target psychosocial functioning in the initial stages of psychosis hold out the prospect of preventing long-term psychosocial disability. These facts about the early trajectories of disability informed the concept of the adolescent and early phase of psychosis as a 'critical period' influencing the longer-term outcome (Birchwood & Macmillan, 1993; Birchwood *et al*., 1998).

Early trajectories of psychosocial functioning: are early interventions being targeted appropriately?

Early Intervention Services (EIS), which provide specialist assertive outreach-style care during the 'critical period' (Birchwood et al., 1998), is considered the 'gold standard' treatment for young people with early psychosis (National Institute of Clinical Excellence - *NICE* guidelines, 2014). Whilst EIS has shown to have substantive benefits in a number of domains, including vocational and educational outcomes (Correll *et al*., 2018; Fowler *et al.*, 2009), a recent large UK EIS cohort study (n=878) showed a large proportion (66%) of young people continue to have a high level of psychosocial disability, despite receiving care under EIS for a period of 12 months following referral for a first episode of psychosis (Hodgekins *et al*., 2015a). Furthermore, the majority (53.6%) of individuals were 'not in education, employment and training' (known as NEET in the UK), and were spending as little as 25 hours a week in meaningful structured activities such as socializing, studying, working, and engaging in leisure activities; this is compared with 60 + hours in healthy peers of a similar age (Hodgekins *et al*., 2015b). Thus, there appears to be a group of individuals whose disability is 'unresponsive' to

standard high quality EIS care embodying NICE approved interventions, strongly suggesting that further targeted interventions are urgently needed to restore social trajectories in a way that enables young people to maximize their life chances.

Poor psychosocial functioning also affects individuals who fulfill criteria for ultra-high risk (UHR) of developing psychosis (Cornblatt *et al*., 2007; Cotter et al., 2014, Heinze *et al*., 2018; Lin *et al*., 2011), with a study showing as many as 50% of UHR individuals meet criteria for social disability (Hodgekins *et al*., 2015b). This underlines the notion that disability in FEP begins before the formal onset. Indeed, higher psychosocial disability has also been associated with increased risk of transition to psychosis in the UHR group (Cornblatt *et al*., 2012; Fusar-Poli *et al*., 2010; Velthorst *et al*., 2010), suggesting that early disability is likely to serve as a risk factor for the development of psychosis (Cornblatt *et al*., 2012). However, studies have emerged which show that many UHR young people remain functionally impaired, *irrespective* of whether they transition to psychosis (Cotter *et al*., 2014; Lin *et al*., 2011). Given the high prevalence of disability in the UHR group, irrespective of their transition to psychosis, this suggests that disability arises for reason other than transition to psychosis.

A recent large naturalistic cohort study of young people with a range of emerging mental health disorders (not exclusively psychosis), revealed that as many as 69% had persistent severe psychosocial disability, despite receiving some form of early intervention care (Iorfino *et al*., 2018). We argue therefore that psychosocial disability is a transdiagnostic issue among young people affected by mental health issues: consistent with findings from FEP samples, a significant amount of heterogeneity in functional outcome has also been observed for individuals with other emerging mental health problems in adolescence; however, for those

who presented with severe functional impairments upon entry to clinical services, their impairments were persistent over the course of treatment (Heinze *et al*., 2018; Hodgekins *et al*., 2015a; Iorfino *et al*., 2018), again showing that for many, these deficits are potentially enduring.

Whilst it is difficult to determine whether and to what degree poor psychosocial functioning is a cause of mental health difficulties, what is clear is that poor psychosocial functioning predates the onset of formal psychotic disorder (Addington & Addington, 1993). Widespread impairments in 'premorbid functioning' – defined as functioning prior to the onset of illness – is typical of individuals who later develop psychosis (Addington & Addington, 2005; Agerbo *et al*., 2004; Hafner & an der Heiden, 1999; Jeppesen *et al*., 2008; Lucas *et al*., 2008; Tandberg *et al*., 2012). Addington & Addington (2005) demonstrated that poor functioning which emerges in childhood and continues on a declining course was the best predictor of psychosocial outcome not only at illness onset, but 2 years after the initiation of treatment. This underlines that for many young people, functional deficits are already in place before psychosis formally manifests, and psychosocial disability apparent at the formal onset of psychosis is simply a continuation of earlier trajectories; these individuals are likely at risk of enduring illness and disability.

Intervention in this premorbid phase may be most effective to prevent long-term disability, but this is likely to prove challenging as these individuals may not come to the attention of clinical services until they present with clinical symptoms. This leads to questions as to whether an 'at risk' group can be identified and targeted by intervention prior to the manifestation of formal psychosis.

Young people with NEET status: a candidate group for prevention of long term psychosocial disability?

The transition from school to employment is a critical time in a young person's life; failure to secure employment or access further training or education by the age of 25 places the individual at high risk of long-term unemployment, deprivation and social exclusion (Rodwell, *et al*., 2018); all of these are known risk factors predisposing individuals to the development of schizophrenia and other non-affective psychoses (Heinz, Deserno & Reininghau, 2013; Kirkbride *et al*., 2012; Van Os *et al*., 2010). It is estimated that around 18% of the 20-24-year group are not in education, employment or training (i.e. NEET: OECD, 2015; Rodwell *et al*., 2018).

Factors such as lower socioeconomic status, motivation, parental unemployment and family fragmentation puts young people at risk of NEET status (Eurofound, 2012; Powell, 2018), suggesting a vicious circle of social disadvantage and heightened risk of developing psychosis. A recent prospective 10-year study looking at predictors of NEET in young people showed that persistent mental health problems in adolescence, disruptive behaviours and frequent cannabis use were associated with a failure to make a successful transition from school to employment, further education or training (Rodwell *et al*., 2018). This raises the possibility that the link between mental health problems and psychosocial disadvantage is bi-directional, where emerging mental health problems are likely to contribute to poor educational attainment and psychosocial outcome, and vice-versa (Gladwell *et al.*, 2016). Young people with NEET status in general are therefore a candidate group for intervention and preventative strategies, and it is conceivable that successful interventions here might well reduce the numbers developing

formal psychosis. Any such intervention would, of course, need to exist outside public health mechanisms to avoid potential medicalizing of psychosocial disadvantage.

Markers of psychosocial disability?

The challenge of determining who to target with preventative interventions and the nature of such interventions is to identify pathological factors or markers that are relevant to specific clinical populations (Strauss & Carpenter, 1977). Early identification of potentially modifiable markers of poor psychosocial outcome holds out the prospect of stratification of targeted interventions to prevent long-term psychosocial disability.

A number of predictors and markers of psychosocial functioning have consistently been identified in psychosis, which include: poor adolescent premorbid adjustment, early appearance of negative symptoms, poor cognitive function, longer duration of untreated psychosis (DUP), early age of onset of psychosis, and male gender (Ayesa-Arriola *et al*., 2013; Lucas *et al*., 2008; Malla & Payne, 2005; Rammou *et al*., 2017; Santesteban-Echarri *et al.*, 2017). Further, there is evidence showing that markers such as impaired cognition and negative symptoms are apparent prior to the onset of illness, making them potential candidate targets to enhance functional improvement (Couture *et al.*, 2006).

Cognitive impairments in psychosis can be considered as those falling within the broader domains of social cognition (SC), defined as the mental operations underlying social interaction (Adolphs, 2009), and neurocognition (NC), which describes a group of cognitive functions implicated in processes such as learning, memory and problem solving. SC and NC

impairments tend to remain stable across the different stages of psychosis (Addington, Saeedi & Addington, 2006; Lee *et al*., 2015; Thompson *et al*., 2012), and deficits are also evident in first-degree relatives of individuals with schizophrenia (Janssen, Krabbendam & van Os, 2003), likely suggesting that poor cognition is a possible trait marker of illness rather than a consequence of illness progression (Allott, Liu, Proffitt, & Killackey, 2011). Further, cognitive deficits are linked with a core of domains of psychosocial functioning in those with enduring psychosis (Fett et al., 2011; Green et al., 2000), first-episode psychosis (Addington *et al.*, 2006; Santesteban-Echarri *et al*., 2017; Stouten *et al*., 2014) and individuals with UHR status (Chung *et al*., 2008; Cotter et al., 2014; Lee *et al*., 2015; Thompson *et al*., 2012). Similarly, persistent negative symptoms are evident in the early course of psychosis (both in UHR and FEP groups) are associated with poor psychosocial outcome (Addington *et al*., 2015; Cornblatt *et al*., 2012; Lin *et al*., 2011; Piskulic *et al*., 2012). These findings indicate that negative symptoms and cognition may be a 'trait' indicator of long term poor functioning in individuals with psychosis, perhaps reflecting neurodevelopmental differences (Lin, Wood, Yung, 2013).

Is there a neurodevelopmental pathway to psychosocial impairment?

Impaired cognition, negative symptoms and poor psychosocial functioning develop long before the onset of frank disorder. These deficits seem to have their origins in adolescence, a critical stage for brain maturation, particularly in the social brain regions (Pantelis & Bartholomeusz, 2014). As we have shown, for some individuals, functioning at formal illness onset reflects an ongoing, often long-standing trajectory, persisting even when psychosis symptoms remit. It has been argued that these findings support a neurodevelopmental hypothesis of psychosis, and this subgroup is perhaps more neurologically impaired than those with good psychosocial functioning and intact cognition (Fenton & McGlashan, 1994; Kirkpatrick *et al*., 2001).

Indeed, the regions of the brain which go through extended development during adolescence are the same as those underpinning social cognition and neurocognition (Bartholomeusz & Allott, 2012; Lin *et al*., 2013). It is on this basis that it has been hypothesised that aberrations in the neurodevelopmental process, linked to cognitive deficits, lie at the heart of early and enduring psychosocial difficulty (Bartholomeusz *et al*., 2011; Blakemore, 2008; McGlashan & Hoffman, 2000). Interventions which are delivered during adolescence are therefore more likely to be more effective given the neuroplasticity of the brain at this stage (Bartholomeusz *et al*., 2011).

However, given that psychosocial impairments develop from an earlier age, one could also argue the reverse: cognitive impairments may be a *secondary* phenomenon arising from reduced or adverse social exposure and modelling during childhood and adolescence. This would require plausible early adverse psychosocial experiences affecting social *and* cognitive development. A link between early adverse childhood experience and anomalous psychosocial outcomes has been demonstrated by Stain and colleagues (2013), who found that childhood trauma was associated with poorer premorbid functioning and later psychosocial impairments in individuals with FEP. Such experiences have been shown in many studies to act as risk factors for psychosis: those who experience childhood trauma are 2.8 times more likely to develop psychosis in adulthood (Varese *et al*., 2012); trauma and neglect feature often in personal histories.

How might such experiences affect social development? Trauma can disrupt attachment mechanisms, in turn affecting interpersonal confidence and engagement which if untreated, are likely to be maintained over time (Stain *et al*., 2013). Early stressors such as childhood

maltreatment can also lead to enduring brain dysfunction, and disrupt the development of cognition (Anda *et al*., 2006). For example, the hippocampus, which has a critical role in learning and memory function, is involved in inhibiting the stress response of the hypothalamic-pituitary-adrenal (HPA) axis through glucocorticoid pathways, but exposure to prolonged stress can disrupt this feedback loop resulting in hyper-reactive HPA response to subsequent normal life stressors (Barker *et al*., 2015). Dysregulation of this system, specifically the corticotropin-releasing hormone (CRH) during stress, influences neuronal structure and hippocampal functions such as memory (Maras & Baram, 2012). Indeed, individuals exposed to childhood maltreatment are shown to have reduced hippocampal volume and lowered cognitive functioning in childhood and adulthood (Anda *et al*., 2006; Bremner, 2003; McCabe *et al*., 2012), further making these individuals more vulnerable to psychosocial impairments. Individuals who experience childhood trauma are therefore at high-risk of long-term psychosocial disability.

Future Directions

Poor psychosocial functioning in young people should be an important intervention target regardless of its diagnostic association. Current symptom-focused early intervention approaches do not seem to affect psychosocial disability and therefore need re-thinking. An early intervention approach that addresses social disability is needed to ensure that disability does not become entrenched. Further, there is a window of opportunity to deliver broad spectrum interventions to young people who are NEET to reduce social disadvantage and marginalisation, and potentially reduce the numbers developing formal psychosis.

Implications for universal interventions to prevent psychosocial disability

As previously discussed, young people with NEET status are a high-risk group where preventative interventions could be targeted to reduce socio-economic disadvantage and thus potentially reduce the numbers developing formal psychosis. However, since psychosocial disadvantage is not a clinical problem, any interventions within this group would have to occur outside health services. For example, the UK government has implemented a number of policies and initiatives to tackle unemployment in young people; these are largely focused on supported vocational interventions (Powell, 2018). Whilst there is strong empirical support for supported vocational interventions in individuals with mental health problems, these interventions are most effective when individuals are motivated, and this type of intervention may not be successful in complex NEET groups (Bond *et al*., 2014, Fowler *et al*., 2017). Interventions targeting motivation, interpersonal skills, and general cognitive skills which are important for obtaining employment (such as planning and decision making), may help to tackle psychosocial impairment in this groups.

Implications for indicated interventions for individuals with psychosis and psychosocial disability

Secondly, there is a need for early indicated intervention in those with established poor premorbid functional trajectories in FEP and those at-risk of developing psychosis. An example of a novel intervention which specifically targets severe psychosocial disability in psychosis is Social Recovery Cognitive Behavioural Therapy (SRCBT; Fowler *et al*., 2009). A recent randomized controlled trial has demonstrated the effectiveness of SRCBT at increasing structured activity in FEP individuals with severe social disability, which had proved unresponsive to standard EIS (Fowler *et al*., 2017). Delivering SRCBT to young people who

already have persistent psychosocial disability when they present to EIS, may help to prevent further decline in functioning and promote social recovery. Further, there is potential for the SRCBT to be refined to incorporate a cognitive remediation or social cognitive intervention in those with such deficits, to test whether this increases response to psychosocial intervention. Finally, interventions aimed at improving attachment and sequelae of trauma may also improve psychosocial functioning for young people.

Conclusion

Psychosocial impairments occur long before the onset of formal mental disorder, and 'untreated disability' seems to have a deleterious effect on outcome. Poor psychosocial functioning affects a number of young people, irrespective of whether they transition to psychosis. Delivering interventions at a universal level to 'at risk' groups, such as young people who fail to make the transition from school to employment or training, may prevent long-term economic disadvantage and social marginalisation, potentially bolstering resilience against the development of severe mental health problems such as psychosis. Further, early indicated intervention for those with persistent poor psychosocial functioning in FEP and UHR groups that address motivation, interpersonal functioning and cognition, may be most effective at improving psychosocial functioning.

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