

Synopsis for EU-GEI Publication

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Preliminary title: Age of onset and premorbid adjustment: are different pattern of cannabis use related to the supposed entities of deficit- and non-deficit-syndrome?
Contact info for the person proposing the synopsis Name: Laura Ferraro Partner no: 17 e-mail address: laura.ferraro@unipa.it
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Working and writing group: Laura Ferraro, Caterina La Cascia, Fabio Seminerio, Cannabis and psychosis group, Palermo EUGEI-TEAM , WP2 sites- authors list, Jim van Os, Bart Rutten, Craig Morgan, Diego Quattrone, Robin M. Murray, Daniele La Barbera, Marta Di Forti
Work Packages involved: wp2
Partners involved from whom candidate co-authors (<i>additional to working and writing group</i>) should be nominated:
Objectives (scientific background, hypothesis, methods, and expected result) Background Several studies show an association between cannabis use and early age of onset of psychotic disorders, particularly schizophrenia (Compton, Broussard, Ramsay, & Stewart, 2011; Donoghue et al., 2014; González-Pinto et al., 2011). A systematic meta-analysis revealed that the age of onset was 2.70 years earlier among patients at their First Episode of Psychosis (FEP) with history of cannabis use than those without ($z = -7.18$; $p < 0.001$) (Large, 2011). In further support of this relationship, an association has also been found between the earlier age of first cannabis use and age of onset of schizophrenia, in patients who used cannabis daily, and especially high-potency cannabis (Di Forti et al., 2014). In two previous studies, we found that FEP patients who smoked cannabis in their lifetime have a better premorbid IQ (Ferraro et al., 2013), a better premorbid social adjustment and a lower premorbid academic adjustment, especially if cannabis lifetime use occurred on a daily-basis (premorbid and cannabis future EUGEI paper by Ferraro et al.), and they also had a lower age of onset of psychosis compared to never-users, as already observed in Di Forti et al (2014). Previous studies have related a better premorbid social adjustment with an earlier age of onset (Cannon-Spoor, Potkin, & Wyatt, 1982; Goldberg et al., 2011; Larsen et al., 2004) and with an acute onset of the illness, while poor premorbid social adjustment is more often related to an insidious onset (Bailer, Bräuer, & Rey, 1996). Additionally, impaired premorbid social functioning is often associated with a higher severity of negative symptoms and poorer post-morbid social functioning (Ayesa-Arriola et al., 2013; Chang et al., 2013; Galderisi et al., 2013; Rabinowitz, De Smedt, Harvey, & Davidson, 2002). It has been proposed that the supposed entity of “Deficit Schizophrenia” or “Negative Syndrome” as opposed to “Non-Deficit Schizophrenia”, is related to male gender (Roy, Maziade, Labbé, & Mérette, 2001), increased presence of familial history of psychosis

(Kirkpatrick, Ross, Walsh, Karkowski, & Kendler, 2000) and poor premorbid adjustment – especially in the social domain (Strauss et al., 2012) – as well as more severe clinical outcome in terms of cognition and symptomatology (Bucci et al., 2015; Carpenter, Heinrichs, & Wagman, 1988; Fenton & McGlashan, 1994; Malaspina et al., 2000).

In this model, age at onset and premorbid functioning are proposed as mediators between gender, familial history of psychosis and clinical outcome (Bucci et al., 2015), in accordance with the notion that the “deficit” entity has a different developmental trajectory, and that premorbid adjustment is one of the essential aspects of its characterization (Galderisi & Maj, 2009; Goldberg et al., 2011).

Even if Kirkpatrick et al. (1996) have initially identified a less severe prevalence of lifetime cannabis use in deficit compared to non deficit syndrome, but no differences in terms of current use (Kirkpatrick et al., 1996), none of the studies on the Deficit Syndrome looked at cannabis use in adolescence as a risk factor for a earlier age of onset (Di Forti et al., 2009, 2014) in non-deficit syndrome, or they merely excluded recent substance abuse (Allen et al., 2013; Bucci et al., 2015; Chang et al., 2013; Strauss et al., 2012).

Hypothesis

Different pattern of cannabis use (heavy-recreational-none/age at first use/THC concentration) could be related to differences similar to those observed between “deficit” and “non-deficit” patients in terms of age of onset and premorbid social and academic adjustment. If this hypothesis is correct, cannabis use could be considered an important risk factor for the development of psychosis in subjects less predisposed that was not considered before in determining the difference between deficit and non-deficit syndrome.

Objectives

To look at a pattern of theoretically-driven markers of liability to schizophrenia similar to those expected in “deficit-syndrome”, compared to “non-deficit syndrome”, such as later age of onset of psychosis, male gender, lower premorbid social adjustment, more cognitive deficits, more negative symptoms and family history of psychosis in a sample of FEP, by testing the hypothesis that different patterns of cannabis use (never-recreational-heavy use) are differently related to these markers. i.e. cannabis-users are “non-deficit” patients compared to cannabis-non users.

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Data needed for the study:

- MRC,
- CEQ,
- PAS,
- WAIS,

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<ul style="list-style-type: none">• FIGS (Family history of psychosis)• SDS (Schedule for Deficit Syndrome-negative symptoms) or OPCRIT
Plan for statistical analysis (overall strategy): Mixed ANCOVA with “age at onset” as dependent variable and a number of predictors as fixed factors: frequency of cannabis use (never-less than everyday-everyday) sociodemographic, IQ -scales, premorbid scores from factorial analysis, SDS scores, family history of psychosis.
Other analyses/methods: will be later planned if necessary (e.g. cox regression)
Involvement of external Parties (non EU-GEI): none
IPR check:
Timeframe: By the end of 2017
Additional comments: