Synopsis no.: *S5.34*

Preliminary title:

Tobacco use of subjects at ultra high risk to develop a first psychotic episode and the association with neurocognition.

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Publication category: 1

Working and writing group:

Hille de Vries, Jentien Vermeulen, Frederike Schirmbeck, Lieuwe de Haan and WP5 author group.

Work Packages involved: WP5

Partners involved from whom candidate co-authors (*additional to working and writing group*) should be nominated:

Objectives (scientific background, hypothesis, methods, and expected results):

Scientific background

Tobacco use is an undisputed risk factor for an increased risk of death in patients with schizophrenia. Adults with schizophrenia were shown to be almost ten (SMR 9.9, 95%CI 9.6-10.2) times as likely to die from Chronic Obstructive Pulmonary Disease (COPD) compared to the general population.[1] Although tobacco smoking has reduced in the general population during the last few decades, rates of smokers in psychiatric populations are still strikingly high. A meta-analysis showed that schizophrenia patients had a higher prevalence of ever smoking than the general population (9 studies across 6 countries, weighted average OR=3.1, CI 2.4-3.8).[2] Apart from the well-known associations of smoking and cardiovascular diseases and cancer, evidence of adverse effects of smoking on neurocognition. Recent studies in adults without a mental disorder show that passive and active smokers are at increased risk for cognitive impairments [3, 4]. Specifically, chronic cigarette smoking is associated with deficiencies in executive functions, general intellectual abilities, learning and/or memory and processing speed [5], most likely explained by smoking related global brain atrophy and structural and biochemical abnormalities in anterior frontal regions, subcortical nuclei and commissural white matter [5]. Although smokers often report to continue smoking because of experienced alleviation of feelings of depression and anxiety and for relaxation as well as relieving stress [6], studies consistently show strong negative associations between smoking and mental health [7, 8]. In patients with schizophrenia, a controversy remains about the positive or negative effect of nicotine on neurocognition. Conflicting hypotheses regarding neurocognition and schizophrenia have been suggested. Pre-clinical evidence has shown that nicotine affects several neurotransmitter systems,

including dopamine (DA), glutamate, and γ-aminobutyric acid (GABA), and certain neuropsychological deficits associated with these neurotransmitters (reaction time, spatial working memory, sustained attention, and sensory gating) are improved after nicotine administration in patients with schizophrenia.[9] These positive effects on neurocognition appear to be more pronounced in smokers with schizophrenia, and may be an important mechanism that explains the co-morbidity of schizophrenia and tobacco dependence. A recent cross-sectional study found that smokers within a SMI population have worse composite neurcognitive outcomes and poorer functional outcome than past or never smokers. [10] In a recently published study we report findings that indicate that smoking is associated with poorer cognitive performance in patients, their siblings, and healthy control subjects compared with nonsmoking. Smoking cessation was found to be significantly associated with an improvement of processing speed in patients [11].
To the best of our knowledge, we will be the first to examine the [cross sectional and longitudinal] association between tobacco use and neurocognitive outcomes in subjects at ultra high risk to develop a first psychotic episode and healthy controls.

Key questions

Question 1.
Is current smoking behaviour associated with performance in specific cognitive domains?

Question 2.
Are smoking and cognitive functioning associated longitudinally and is change in tobacco use associated with change in performance in specific cognitive domains?

Methods and expected results

Cross-sectional and longitudinal data collected to assess tobacco use and neurocognitive functioning in individuals at risk for psychosis and healthy controls will be used. To account for possible confounding effects we will control for psychopathology, cannabis use, medication, socioeconomic status, childhood trauma and general functioning.

Data will be analyzed using linear mixed-effects analyses to examine the relationship between tobacco use and neurocognitive outcomes. If possible in terms of appropriate fit indices, cross-lagged panel analyses will be used to explore the direction of the association.

We hypothesize that tobacco use is associated with reduced cognitive functioning compared to non-smokers and that smoking cessation is associated with improvement in cognitive functioning.

- Specifically we expect processing speed, working memory, verbal learning, visual-spatial ability and cognitive flexibility to be negatively associated with smoking.
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Prospective UHR data needed for the study:

- Tobacco use
- Neuropsychology: processing speed as measured with the WAIS symbol-coding, working memory as measured with the Digital Span score, verbal learning as measured with the Auditory Verbal Learning Test, visual-spatial ability as measured with the WAIS block design and cognitive flexibility as measured with the TMT.
- Covariates; Psychopathology (CAARMS, BPRS, MADRS), socioeconomic status (education (highest level and years), employment and income)), GAF, trauma (CTQ) cannabis and medication use.

Other analyses/methods:

N/A
Involvement of external Parties (non EU-GEI): none
IPR check:
Timeframe: Month 2: Literature search; obtaining, merging, checking, cleaning of data Month 4: Completion of statistical analysis and first draft of manuscript Month 6: Manuscript submission
Additional comments: N/A

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