Synopsis for EU-GEI WP5 Publication

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Preliminary title: Pathways from speech illusions to psychotic symptoms in subjects at ultra-high risk for psychosis: combining an experimental paradigm of aberrant experiences with network analysis

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Working and writing group: The Netherlands, site Amsterdam AMC-UvA

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Work Packages involved:
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EU-GEI Partners involved from whom candidate co-authors (*additional to working and writing group*) should be nominated:
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Objectives (scientific background, hypothesis, methods, and expected results):
One of the oldest and most influential theories of delusion formation is that delusions arise in an attempt to explain unusual experiences (James, 1890; Reed, 1972; Maher, 1974, 1988). Unusual experiences may refer to external events, such as a social interaction, or to internal experiences, such as a bodily sensation or perceptual aberration. According to the aberrant salience theory (Kapur, 2003), in the development of psychosis events and experiences become filled with an augmented sense of significance -i.e. are perceived as 'unusual'- due to a dysregulated, hyperdopaminergic state.
Kapur (2003) conceptualises hallucinations as a direct experience of the aberrant salience of internal representations, and delusions as a cognitive effort to make sense of these experiences.
The findings of several epidemiological studies confirm that in a non-clinical population hallucinatory experiences often precede delusional ideation (Krabbendam et al, 2004; Smeets et al, 2012) and that their co-occurrence enhances the risk of transition to clinical psychosis, particularly when combined with negative emotional states (Hanssen et al, 2005; Krabbendam et al, 2005). Cognitive impairment has also been identified as a marker for transition to psychosis (Fusar-Poli, 2012).

The White Noise Task (Galdos et al, 2011) was developed as an experimental task to assess the tendency to attribute meaning and emotional value to random auditory stimuli: whether individuals experience speech illusions in white noise and if so, their subsequent evaluation of neutral versus affective content. Two studies to date have demonstrated that particularly speech illusions with affective content as assessed with the White Noise Task are associated with (a composite measure of) positive symptoms in adult patients with psychotic disorders, also when controlling for cognitive impairment (Galdos et al, 2011; Catalan et al, 2014). However, findings regarding (a composite measure of) subclinical positive symptoms in non-patients were inconsistent. Galdos et al (2011) found an association in a younger and larger non-clinical sample, whereas Catalan et al (2014) did not.
A recent study of the White Noise Task in a large sample of 11-12 year old children demonstrated that speech illusions with affective content are associated with hallucinations, negative affect and a proxy

measure for cognitive ability in this sample, but not with delusions or a family history of mental illness (Rimvall et al, 2016). By contrast, Galdos et al (2011) found indication for a higher rate of speech illusions in siblings of patients with psychotic disorders compared to controls, indicating a link with familial vulnerability for psychosis.

Currently, further research is required to examine whether speech illusions as assessed with the White Noise Task are indicative of psychosis liability, and to explore underlying mechanisms. By using a composite measure–i.e. a sum-score of symptoms–information about specific relations between speech illusions and individual psychotic symptoms is discarded. In an attempt to overcome such limitations, network analysis (Borsboom & Cramer, 2010) is an alternative framework focused on identifying relations between individual symptoms or components of a disorder. We argue that further research would highly benefit from a symptom-based network approach and examination in an ultra-high risk population.

Consequently, our research questions are:

1) Are there differences in the subclinical psychotic symptom networks between UHR subjects who do and do not experience speech illusions, and between those who experience illusions with affective versus neutral content?
2) What are the pathways (cross-sectional) between speech illusions and subclinical positive symptoms?
3) What are the pathways (prospective) between speech illusions and transition to clinical psychosis?

Our expectations are:

Ad 1) If feasible, mainly if sufficient N: we expect higher connectivity of the subclinical psychotic symptom networks of UHR subjects with versus without speech illusions as assessed with the White Noise Task, and again for subjects experiencing affective versus neutral content of speech illusions.

Ad 2) Partly explorative. We expect to find multiple pathways between speech illusions and subclinical positive symptoms, among which a pathway to delusional ideation through hallucinatory experiences. We will explore whether affective states and cognitive deficits are mediating items.

Ad 3) Partly explorative. We expect to find multiple pathways between speech illusions and clinical psychosis, among which a pathway speech illusions -> hallucinatory experiences –> delusional ideation –> clinical psychosis. Again, we will explore whether affective states and cognitive deficits are mediating items.

Data needed for the study: (please list the EU-GEI WP5 instruments)

- White Noise Task
- BPRS
- CAARMS

Plan for statistical analysis (overall strategy):

Network analysis (Borsboom & Cramer, 2013): comparison of network structures (Van Borkulo et al, 2016), examination of centrality measures (Barrat et al, 2004; Bocaletti et al, 2006; Opsahl et al, 2010) and examination of shortest pathways (Brandes, 2008; Isvoranu et al., 2016) in R.

Other analyses/methods:

N/A

Involvement of external Parties (non EU-GEI):

University of Amsterdam, Methodology department

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IPR check (Intellectual property rights): N/A
Timeframe: Once the data is received it's expected that data analyses will take approximately 4 months and drafting of the paper will take approximately 4 months.
Additional comments: N/A