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**Background:** Exposure to infectious microorganisms has been implicated as an important risk factor in the development of psychotic disorders. Epidemiological and laboratory evidence suggests that exposure at various developmental periods may increase psychosis risk, from in utero through to childhood and adult life. Individuals who meet clinical high risk (CHR) criteria are at substantially increased risk of developing a psychotic disorder; however, no study to date has explored whether exposure to schizophrenia-associated pathogens is associated with clinical outcomes in this population.
**Methods:** Plasma samples from 254 subjects at ultra-high risk of psychosis from the EU-GEI cohort and 116 age- and sex-matched controls were tested for antibodies to the following infectious organisms: Toxoplasma gondii, herpes simplex virus type 1, cytomegalovirus, Epstein-Barr virus (EBV) and influenza. Samples were also tested for antibodies to the NMDA receptor using a fixed cell-based assay and for levels of S100B (a putative marker of blood-brain barrier disruption) and complement pathway protein expression.
Only pathogens which predicted case-control status were taken through to further analysis looking at symptomatic associations and clinical outcome measures, which included the Positive and Negative Symptom Scale (PANSS), the Scale for Assessment of Negative Symptoms (SANS) and Global Assessment of Function (GAF).
**Results:** In logistic regression analysis, exposure to Toxoplasma was associated with increased risk of meeting CHR criteria (OR 2.66; p = 0.04), whereas EBV exposure was associated with decreased risk of meeting CHR criteria (OR 0.34; p = 0.006). Toxoplasma IgG antibody status was associated with higher SANS scores (p = 0.032) and higher GAF symptoms (p = 0.003) and disability scores (p = 0.003). EBV antibody status was associated with lower GAF scores (p = 0.007), indicating better functioning. In clinical outcome analysis, EBV antibody positivity was associated with a reduced risk of transition to psychosis (OR 0.44; p = 0.04), whereas Toxoplasma IgG seropositivity was associated with poorer functional outcomes at follow-up.
The presence of NMDAR autoantibodies was associated with higher Toxoplasma IgM (p = 0.024), but not IgG (p = 0.972), titres. Furthermore, Toxoplasma IgM was associated with increased levels of serum S100B (p = 0.007) and with increased expression of Complement C4 (p = 0.018, FDR corrected), both of which have been independently implicated in psychosis risk.
**Discussion:** Toxoplasma exposure is associated with severity of negative symptoms and poor functional outcomes in CHR individuals, consistent with the known associations of Toxoplasma exposure in psychotic patients. Specific mechanisms by which Toxoplasma exposure might confer risk of poor outcomes include activation of specific complement pathway proteins, disruption of the blood-brain barrier and infection-induced production of brain-reactive autoantibodies. EBV exposure appears to have a mitigating effect, symptomatically and in terms of outcome, in this population, and as such may represent one of the first reported neurobiological protective factors for the CHR state and for the subsequent development of psychosis.

## O10.4. LATENT INHIBITION AS A STRATIFICATION TOOL FOR SCHIZOPHRENIA DRUG DEVELOPMENT

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**Background:** Stratified medicine approaches have potential to dramatically improve the efficacy of drug development for schizophrenia and other psychiatric conditions, as they have for cancer. Such methods require accurate biomarkers that define populations of patients with a common neurobiological underpinning, for whom a particular treatment is more likely to be effective. Latent inhibition, a learning phenomenon known to be disrupted in schizophrenia, is a good candidate biomarker. Previous studies have shown that LI is typically impaired in positive symptomatic patients and remediated with dopamine blocking therapies, but accentuated in negative and cognitively symptomatic patients that anti-psychotics are largely ineffective for. Computerised LI assessment may therefore be a simple non-invasive means to differentiate patients with differing neurochemical states and/or etiologies.
**Methods:** We modified Granger et al's (2016) LI task to allow web-based delivery on the CANTAB Connect software platform. We tested the validity and repeatability of the task in inducing LI behaviour in a total of 200 individuals recruited and assessed online via Prolific. To assess sensitivity of the task to a pro-cognitive pharmacological manipulation, we compared LI in 20 healthy non-smoking volunteers who received a dose of 2mg nicotine or placebo via mouth spray in a double-blind crossover design with two-day washout. To assess task sensitivity to a clinical model, we compared LI in 30 healthy volunteers administered either 7.5% $CO_2$ or medical air in an anxiety induced dopamine release protocol, again in a double-blind crossover design, with 30-minute washout between gas inhalations.
**Results:** LI was reliably demonstrated in a 6-minute task administered via the web to remote participants. Administration of nicotine, but not placebo, enhanced latent inhibition (p<.05). Conversely, inhalation of $CO_2$, but not medical air, raised self-reported anxiety and impaired latent inhibition (p<.05).
**Discussion:** This brief task appears to elicit a reliable measure of LI in both remote and in-person assessments. Initial experimental studies suggest it has strong potential as a biomarker that is modified by both pharmacologically (nicotinic) and clinically-relevant (dopaminergic) manipulations. Further studies should assess whether LI can help accelerate or rationalise non-typical treatment strategies for patients with psychotic disorders who do not respond to dopaminergic therapies.

## O10.5. META-ANALYSIS OF CYTOKINE LEVELS AND PSYCHOPATHOLOGY IN SCHIZOPHRENIA

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**Background:** Schizophrenia is associated with aberrant blood levels of inflammatory markers. There is some evidence that treatment with adjunctive anti-inflammatory medications in schizophrenia may be associated with improvement in psychopathology, particularly in patients with abnormal levels of inflammatory markers. However, relationships between inflammatory marker levels and psychopathology in schizophrenia have not been systematically investigated. We performed a meta-analysis of the correlation between blood cytokine levels and psychopathology in schizophrenia.
**Methods:** We identified articles by systematic searches of PubMed, PsycINFO, and Web of Science databases, and the reference lists of identified studies. We included studies, in English, that reported correlations between blood inflammatory markers and psychopathology scores in patients with schizophrenia or provided previously unpublished correlative data. Out of 246 potential studies, 73 studies, comprising 6112 patients, met inclusion criteria. 38% of included studies provided at least some previously unpublished data. Data were pooled using a random effects approach.
**Results:** In all studies, C-reactive protein (CRP) and interleukin (IL)-18 were significantly correlated with multiple domains of psychopathology (effect sizes [ESs]=0.17–0.25). In inpatients, IL-6, CRP, IL-17, IL-18, and interferon (IFN)-γ were significantly correlated with multiple domains