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The association between toxoplasma and the psychosis continuum in a general population setting

Maija Lindgren [a,*], Minna Torniainen-Holm [a,b], Tommi Härkänen [c], Faith Dickerson [d], Robert H. Yolken [e], Jaana Suvisaari [a]

[a] National Institute for Health and Welfare (THL), Mental Health Unit, Finland
[b] Institute for Molecular Medicine Finland (FIMM), Helsinki, Finland
[c] National Institute for Health and Welfare (THL), Health Monitoring Unit, Finland
[d] Stanley Research Program, Sheppard Pratt Health System, Baltimore, MD, USA
[e] Stanley Division of Developmental Neurovirology, Department of Pediatrics, John Hopkins University School of Medicine, Baltimore, MD, USA

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ABSTRACT

Toxoplasma gondii infection is associated with increased risk for psychosis. However, the possible association between *T. gondii* and psychotic-like symptoms in the general adult population is unknown.

We investigated whether *T. gondii* is associated with psychotic-like symptoms and psychosis diagnoses using data from Health 2000, a large cross-sectional health survey of the Finnish general population aged 30 and above. Seropositivity to toxoplasma was defined as a cutoff of 50 IU/ml of IgG antibodies. Lifetime psychotic-like symptoms were identified with section G of the Composite International Diagnostic Interview, Munich version (M-CIDI). Symptoms were considered clinically relevant if they caused distress or help-seeking or there were at least three of them. Lifetime psychotic disorders were screened from the sample and were diagnosed with DSM-IV using SCID-I interview and information from medical records. All data were available for 5906 participants. We adjusted for variables related to *T. gondii* seropositivity (age, gender, education, region of residence, cat ownership, and C-reactive protein measuring inflammation) in regression models.

We found that *T. gondii* seropositivity was significantly associated with clinically relevant psychotic-like symptoms (OR 1.77, $p = 0.001$) and with the number of psychotic-like symptoms (IRR = 1.55, $p = 0.001$). The association between toxoplasma and diagnosed psychotic disorders did not reach statistical significance (OR 1.45 for schizophrenia).

In a large sample representing the whole Finnish adult population, we found that serological evidence of toxoplasma infection predicted psychotic-like symptoms, independent of demographic factors and levels of C-reactive protein. Toxoplasma infection may be a risk factor for manifestation of psychotic-like symptoms.

1. Introduction

Toxoplasma gondii (*T. gondii*) infection is associated with increased risk of psychosis (Yolken and Torrey, 2008). In a recent meta-analysis, *T. gondii* seropositivity was associated with schizophrenia (odds ratio (OR) 1.8, 95% confidence interval (CI) 1.5–2.2) and with bipolar disorder (OR 1.5, 95% CI 1.1–2.2) (Sutterland et al., 2015). The OR was higher in patients with recent-onset than in chronic schizophrenia. High serointensity was associated with higher odds of schizophrenia, and the OR also varied by region, decreasing with higher seroprevalence in the population (Sutterland et al., 2015).

Increased risk of toxoplasma infection *before* the onset of schizophrenia was reported in the meta-analysis by Sutterland et al. (2015) with 1.3 OR (95% CI 1.1–1.6). However, fewer studies have investigated whether *T. gondii* is associated with subclinical psychotic-like symptoms, which may indicate subsequent psychosis risk (Schultze-Lutter et al., 2015). High serointensity associated with higher OR for schizophrenia, and the OR also varied by region and by the seroprevalence in the general population. In a Dutch adolescent population-based cohort study, toxoplasma was not associated with subclinical psychotic symptoms (Wang et al., 2011). In contrast, in young people at ultra-high risk (UHR) for psychosis, seropositivity to *T. gondii* related to more severe psychiatric symptoms and positive symptoms (Amminger et al., 2007).

In this study, we used data from a large Finnish general population survey to investigate whether *T. gondii* seropositivity and serointensity are associated with psychotic disorders and with subclinical

* Corresponding author at: National Institute for Health and Welfare, Mental Health Unit, PO Box 30, FIN-00271 Helsinki, Finland.
E-mail address: maija.lindgren@thl.fi (M. Lindgren).

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psychotic-like symptoms. Thus, we looked at psychotic symptoms distributed along a continuum at varying levels of severity (van Os et al., 2009).

2. Methods

2.1. Participants

Data used in this study was from the Health 2000 (BRIF8901), a nationally representative survey of the Finnish population conducted in 2000–2001 (Aromaa and Koskinen, 2004). Adults aged 30 years and over were sampled using stratified two-staged cluster sampling ($N = 8028$). Individuals were chosen to the study to be representative of their age and gender group in the area where they lived. The protocol included a home interview and health examination at the local health care center or, for those unable to attend, a condensed interview and health examination at home or in an institution (Aromaa and Koskinen, 2004). Fig. 1 shows the participant flow diagram in the Health 2000 survey.

All participants gave written informed consent and the study was approved by the ethics committees of the Hospital District of Helsinki and Uusimaa and the National Institute for Health and Welfare.

2.2. Toxoplasma

Plasma samples were collected as a part of the participants' health examination. Immunoglobulin G (IgG) antibodies against *T. gondii*, indicating previous infection, were performed by solid phase enzyme immunoassay. Whole tachyzoite lysate from Ross South Labs, Spanish Fork Utah, USA was used, employing methods as previously described by Dickerson et al. (2007). Comparisons to standards with known levels of antibody were used to convert sample values to international units. We used 50 IU/ml as the cut-off for seropositivity, as in Sugden et al. (2016). In addition, serointensity, defined as the quantitative level of antibody in IU/ml, was analyzed as a continuous variable.

2.3. Psychotic-like symptoms

Lifetime psychotic-like symptoms were assessed using the Finnish translation of the Composite International Diagnostic Interview, Munich version (M-CIDI) (Wittchen et al., 1998), which was a part of the health examination (Pirkola et al., 2005).

Psychotic-like symptoms were assessed in section G of the interview. Participants were shown with a list of 23 psychotic-like experiences (Table 1) and asked if they had ever experienced any of them. Five of the experiences are hallucinatory (17–21) and 16 delusional (1–14), with two symptoms (22 and 22A) probing catatonic-like symptoms.

If any of the presented symptoms were endorsed, questions concerning the clinical relevance of the experiences were asked. Using a previously formed definition (Perälä et al., 2007), symptoms were considered clinically relevant if the person reported at least three symptoms, if the person had discussed the symptom(s) with a doctor or other professional, or if the symptom(s) had interfered with normal life.

In addition, the number of psychotic-like experiences reported by the person (0–23 symptoms) was used as a continuous variable in this study.

2.4. Psychotic disorders

Lifetime psychotic disorders were identified from the Psychoses in Finland study, which was a substudy of the Health 2000 survey (Perälä et al., 2007). Psychotic disorders were screened from the Health 2000 sample using the M-CIDI (clinically relevant symptoms as defined earlier), self-reported diagnoses, medical examination, and national register. The register screen included hospital treatment because of a diagnosis of any psychotic or bipolar disorder, free outpatient antipsychotic medication for severe psychotic and other severe mental disorders, and disability

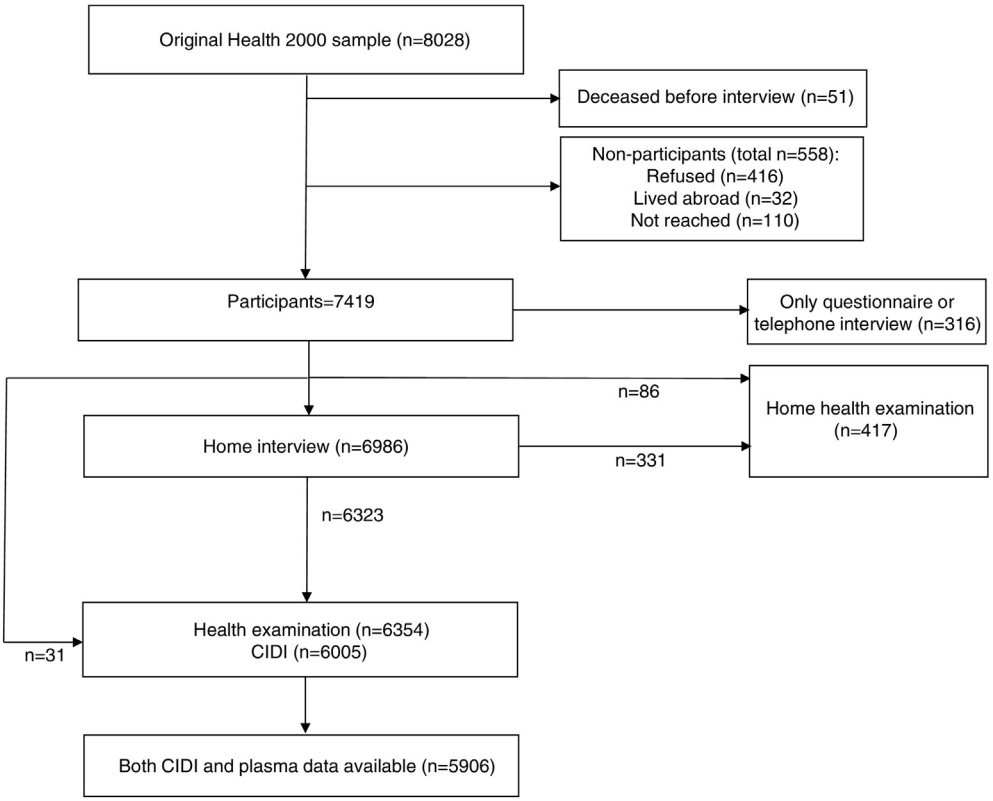

Fig. 1. Participant flow diagram in the Health 2000 study.

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