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The association between childhood *Toxoplasma gondii*, psychotic experiences and grey matter volume: A population-based cohort study

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ABSTRACT

Toxoplasma gondii (*T. gondii*), a parasite that can be transmitted to humans by cats, has been proposed as a modifiable risk factor for schizophrenia and related disorders. However, much of the research examining this relationship has relied on cat ownership as a proxy measure for *T. gondii* exposure. This study examined the relationship between serum *T. gondii* levels and later psychotic experiences (PEs) and brain volume. We also explored the relationship between cat ownership and *T. gondii* serology. Using the Avon Longitudinal Study of Parents and Children (ALSPAC), we studied 3542 individuals for whom data on serum *T. gondii* during childhood and PEs at age 18 were available. Voxel-based morphometry assessed whether MRI measures of grey matter volume at age 20 were associated with *T. gondii* levels among a subset of the participants ($N = 334$). Serum *T. gondii* was not associated with PE group in adjusted models (suspected PEs risk ratio (RR) = 1.06, 95% confidence interval (CI) [0.89–1.27]; definite PEs $RR = 0.86$, 95% CI [0.65–1.13]; psychotic disorder $RR = 1.00$, 95% CI [0.73–1.38]). Exposure to cats during gestation was associated with higher *T. gondii* in adolescence ($\beta = 0.08$, $p = 0.033$), while exposure to cats during childhood was not ($\beta = 0.05$, $p = 0.310$). *T. gondii* was not associated with grey matter volume in the neuroimaging sample ($pFWEs \geq 0.882$, $Zs \leq 3.86$). Future work examining the relationship between *T. gondii* and schizophrenia-spectrum disorders should focus on serology or cat ownership during gestation as a proxy measure of *T. gondii* exposure, as there was no association between childhood cat ownership and *T. gondii*.

1. Introduction

Toxoplasma gondii (*T. gondii*) has been put forward as an environmental factor associated with an increased risk of developing schizophrenia and other psychotic disorders in adulthood (Maisarah et al., 2022; Torrey, 2022; Zhu et al., 2024). *T. gondii* is a protozoan parasite to which most endothermic organisms, including humans, are susceptible, and whose definitive hosts include cats and other felines (Webster et al., 2013). In humans, infection can occur through various routes, including maternal-infant transmission in utero, ingestion of tissue cysts from undercooked meat of infected animals, or ingestion of the parasite's oocysts from food or water contaminated with cat faeces (Maisarah et al., 2022; Tenter et al., 2000).

Much of the evidence in support of the association between the parasite and schizophrenia comes from research in which cat ownership, particularly in childhood, is used as a proxy measure for exposure to *T. gondii*. A recent meta-analysis reported a pooled odds ratio of 2.44 (95% confidence intervals: 1.59–3.73, adjusted) for the association between cat ownership and developing schizophrenia-related disorders (McGrath et al., 2024). However, the majority of the studies included used retrospective case-control designs, which are susceptible to spurious associations due to their vulnerability to recall bias. Moreover, cat ownership is not a perfect proxy measure for *T. gondii* exposure, and prospective population research with serological measures directly examining the relationship between *T. gondii* and psychosis is limited. Several meta-analyses of the association between *T. gondii* serology and psychosis published in the last decade have reported odds ratios ranging between 1.68 and 1.91 (Contopoulos-Ioannidis et al., 2022; Monroe et al., 2015; Oncu-Oner and Can, 2022; Sutterland et al., 2020). Importantly, these meta-analyses all detected evidence of publication

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bias across the literature and did not assess the quality and risk of bias of the individual studies, many of which were retrospective case-control studies that did not adjust for relevant confounders.

Psychotic experiences (PEs), such as delusions, hallucinations, and thought interference, occur in 5–10% of the general population and are associated with an increased risk of developing later mental disorders including psychosis. One study examining the relationship between PEs and cat ownership in childhood did not find a significant association between cat ownership during gestation or at ages 4 and 10 years and PEs at age 18 after adjusting for sociodemographic and socioeconomic factors (Solmi et al., 2017). Given that *T. gondii* exposure is influenced by factors other than cat ownership, it is important to examine the relationship between PEs and serum *T. gondii* specifically, in order to directly establish the role of *T. gondii* as a risk factor.

The current study therefore sought to examine the relationship between serum *T. gondii* at ages 7 to 15 and PEs at 18 years using longitudinal data from the Avon Longitudinal Parents and Children (ALSPAC) sample. To assess whether the effects of *T. gondii* exposure are specific to psychotic symptoms or represent a risk factor for psychopathology more generally, we also examined whether serum *T. gondii* was associated with depression symptoms or diagnosis at age 17. To examine the validity of the use of cat ownership as a proxy measure for *T. gondii* exposure, we investigated the relationship between cat ownership and serum *T. gondii* and/or PEs. In addition, we assessed whether household crowding moderated the relationship between cat ownership and serum *T. gondii* levels, as this has not been examined in prior research (Solmi et al., 2017) and individuals living in crowded households may be in closer contact with house cats and therefore more likely to be contaminated by the parasite. Finally, to probe the mechanisms through which *T. gondii* may increase risk of schizophrenia, we examined the relationship between *T. gondii* serology in childhood and grey matter volume at age 20 in a subset of the ALSPAC sample who took part in previous neuroimaging sub-studies.

2. Methods

2.1. Sample

The ALSPAC sample is a population-based birth cohort from the South West of England recruited in 1990–91 (http://www.bristol.ac.uk/alspac/) (Niarchou et al., 2015). The study originally recruited 14,541 pregnant women who were residents of the study catchment areas and whose expected delivery dates were between April 1st 1991 and December 31st 1992. Additional children were subsequently recruited into the cohort. The total sample size for analyses using data collected after the age of seven is therefore 15,447 pregnancies, resulting in 15,658 foetuses. Sample characteristics and methodology have been previously described (Boyd et al., 2013; Fraser et al., 2013). The cohort has garnered a wealth of data from repeated data-collection sweeps ('clinics') including biological samples, social and demographics factors, physical, educational and mental health outcomes. Ethical approval for the study was obtained from the ALSPAC Ethics and Law Committee. Informed consent for the use of all data collected was obtained from participants following the recommendations of the ALSPAC Ethics and Law Committee at the time. Participants can contact the study team at any time to retrospectively withdraw consent for their data to be used. Study participation is voluntary and during all data collection sweeps, information was provided on the intended use of data.

This study combines neuroimaging data from a study recruiting ALSPAC participants based on PE score (David study $N = 252$) (Drakesmith et al., 2016a, 2016b, 2015; Fonville et al., 2019, 2015), as well as from an overlapping sample recruited for a study based on polygenic risk scores (Linden study $N = 196$) (Lancaster et al., 2019), with 14 participants taking part in both studies. Participants provided informed consent prior to scanning and received financial compensation. Approval was granted by Cardiff University and the ALSPAC ethics Committees. Magnetic resonance imaging was carried out at age 20 years in 413 participants, of whom 334 had data on *T. gondii*. Of these, 105 had PEs and 229 did not.

2.2. Measures

PEs were assessed using the Psychosis-Like Symptoms Interview (PLIKSi) (Zammit et al., 2013) at age 17–18 years. PEs were rated as (a) absent; (b) suspected; (c) definitely present; or (d) psychotic disorder, all following a semi-structured interview based on the Schedules for Clinical Assessment in Neuropsychiatry version 2.0 (World Health Organization, 1994) by a trained psychologist. The latter category was defined as definite PEs that occurred at least once per month over the preceding 6-month period and either caused severe distress, had a markedly negative impact on social or occupational function, or led to help seeking (Zammit et al., 2013).

Depression symptoms were assessed at age 17, participants were classified as a) had no symptoms or diagnosis of depression; or b) had symptoms or diagnosis of depression, which was defined as either having any ICD-10 diagnosis of depression or a score of more than 12 overall and a score of 4 or more on depressive symptom items on the Clinical Interview Schedule-Revised (CIS-R) (Lewis et al., 1992).

Cat ownership was assessed through maternal report at the following ages: 8 weeks gestation, 8 months, 33 months, and 47 months. At each time point, mothers were asked whether they had any pets and to report the number of cats they owned. If mothers reported owning at least one cat at any of the childhood time points (8, 33, or 47 months), participants were coded as having owned a cat in childhood. Conversely, participants were coded as not having owned a cat if mothers answered "no" at all-time points for which data were available (i.e., "no" at every observed time point, with any other time points missing). Participants with missing pet ownership data at all four timepoints were coded as missing. Cat ownership during gestation was analysed as a separate variable: participants were coded as having been exposed to a cat during gestation if their mother reported owning at least one cat at 8 weeks gestation.

Household crowding was calculated based on mothers' reports of the number of people living in the home, the number of living rooms and bedrooms, and whether the home had a kitchen with space to sit and eat, at 8 weeks gestation, 8 months, 21 months, and 33 months. Crowding was then calculated with the following formula:

$$\textit{Household crowding} = \frac{\textit{No.of adults and children living in the home}}{\textit{No.of living rooms} + \textit{no.of bedrooms} + \textit{no.of kitchens to sit/eat}}$$

The crowding variables at 8 months, 21 months, and 33 months were averaged to obtain a single measure of household crowding in childhood.

Maternal marital status was reported by the mother at 8 weeks gestation and recoded into married (first, second, or third marriage) or unmarried (never married, widowed, divorced, separated). Maternal

socioeconomic status was based on self-reported present or last main job at 32 weeks gestation, coded using the UK National Office of Population Censuses and Surveys (OPCS) job codes, from which social class categorisation was derived (manual vs non-manual social class). Highest maternal education was obtained via self-report at 32 months and coded into higher education (degree) or no higher education (CSE/none, vocational, O level, A level). Maternal age was self-reported at 8 weeks gestation, and child's sex was obtained from birth notifications sent to the study centre. The ALSPAC study website contains details of all the data that is available through a fully searchable data dictionary and variable search tool (http://www.bristol.ac.uk/alspac/researchers/our-data/).

2.3. Toxoplasma gondii ELISA

Blood samples were taken during the following ALSPAC clinics: 7 years ("Focus @7" clinic) collected between September 1998 and October 2000; 11 years ("Focus 11+" clinic) collected between January 2003 and January 2005; 15 years ("TeenFocus 3" clinic) collected between October 2006 and November 2008. For individuals with *T. gondii* data at several ages, data from only one of the clinics in the following order of prioritisation were used, based on maximising the number of individuals with serology data at each time: 11 years, 15 years, 7 years.

Whole blood samples were collected and processed by centrifugation at 3500 rpm for 10 min at 4–5 °C. The plasma fraction from the whole blood was then aliquoted out and stored at −20 °C temporarily before being stored long-term at −70/80 °C. For analysis, EDTA plasma samples were plated out into 96-well plates. Enzyme-linked immunosorbent assay (ELISA) was performed using *T. gondii* antigens (Mitchell et al., 2018).

The primary analyses examined *T. gondii* exposure as a continuous variable (serum levels in optical density ratio to standard z-score), with secondary analyses using a binary exposure definition. Because ALSPAC ELISA values are not calibrated to international IgG units, we created a cohort-relative binary indicator in which "elevated" *T. gondii* was defined as values ≥1 SD above the sample mean. While this measure does not represent a validated seropositivity threshold, it allows for internal comparison between individuals with relatively higher versus lower antibody levels.

2.4. MRI

MRI data were acquired at the Cardiff University Brain Imaging Centre (CUBRIC) on a 3T scanner (Signa HDx;GE Medical Systems) using an 8-channel head coil for radiofrequency reception. A high-resolution, 3D fast spoiled gradient-echo (FSPGR) T1-weighted isotropic image was oriented to the AC_PC line (TR = 7.8 ms, TE = 3 ms, inversion time = 450 ms, flip angle = 20°, field of view = 256 mm × 256 mm × 192 mm, 1 mm isotropic resolution) to assess grey matter volume.

2.5. Voxel-based morphometry

Structural MRI was used to derive grey matter volume measures for all participants. These were quantified using standard voxel-based morphometry (VBM) procedures implemented in the Computational Anatomy Toolbox (CAT12) for Statistical Parametric Mapping (SPM12). Images were segmented into grey matter, white matter, and cerebrospinal fluid using the Computational Anatomy Toolbox (CAT12, http://dbm.neuro.uni-jena.de/cat12/) for SPM 12. To ensure all images were aligned to a common anatomical template, grey matter segments were normalised using the Diffeomorphic Anatomical Registration Through Exponentiated Lie Algebra (DARTEL) procedure. To preserve quantitative information about regional tissue volume, normalised grey matter maps were modulated by the Jacobian determinants of the deformation fields. 'Modulated' grey matter volume images were smoothed using a 8 mm full-width at half-maximum Gaussian kernel. CAT12's automated quality assurance tools were used to evaluate image quality. This included assessment of image noise, intensity inhomogeneity, and segmentation accuracy. After automated QC, all scans were visually inspected to confirm satisfactory segmentation and normalisation.

2.6. Statistical analysis

We examined the association between continuous serum *T. gondii* levels and PE severity (no PEs vs suspected PEs, definite PEs or psychotic disorder) using univariable and multivariable multinomial logistic regression models. As a sensitivity analysis, we also investigated the association between binary *T. gondii* exposure (low vs elevated serum *T. gondii*, defined as ≥1 SD above the sample mean) and any PEs (absent vs present) using binomial logistic regression models. Logistic regression models were also used to investigate the association between continuous serum *T. gondii* levels and depression.

A linear regression model was used to examine the association between mother's cat ownership during pregnancy (8 weeks) or during the child's early years (8 months, 33 months or 47 months) and child's serum *T. gondii* levels in late childhood and adolescence (ages 7–15). Both univariable models and multivariable models – adjusting for sex, age at which serology data was collected, maternal marital status, maternal socioeconomic status, maternal education, maternal age at child's birth – were fitted for all the above analyses. The associations with cat ownership were conducted separately for cat ownership during gestation (8 weeks) and during childhood (8 months, 33 months or 47 months). Additionally, interaction terms between cat ownership and household crowding were included in separate models to investigate whether the association between cat ownership and *T. gondii* serology levels differed by levels of household crowding. All analyses were conducted in *R* (version 4.4.0).

For the grey matter volume analysis, voxel-wise comparisons of modulated grey matter images were performed using a general linear model to examine the association between serum *T. gondii* IgG levels and grey matter volume at each voxel across the entire neuroimaging sample. Age, sex, antipsychotic medication, and total intracranial volume (TIV) were included as covariates in the model. Statistical thresholds were set at $p < 0.001$ uncorrected at the voxel level, together with a family-wise error (FWE) correction for multiple comparisons at $pFWE < 0.05$ at the cluster level. These analyses were conducted using SPM 12.

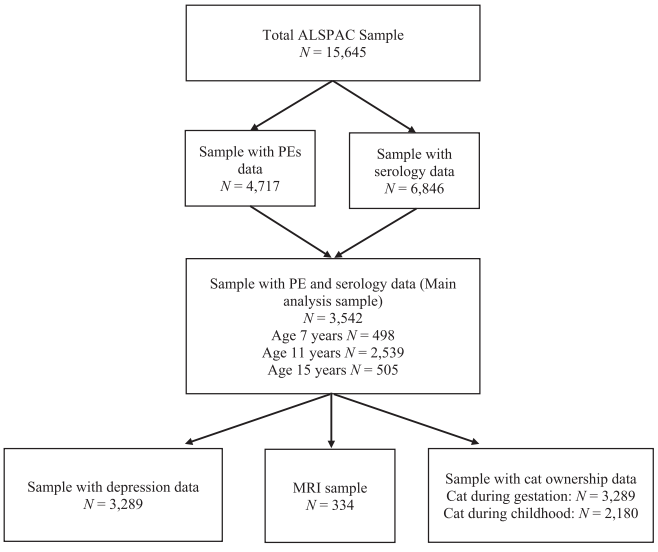

Fig. 1. Flow-chart of sample included in analysis samples.

Table 1
Demographic characteristics by psychotic experiences groups.

	None (N = 3243)	Suspected (N = 132)	Definite (N = 109)	Psychotic disorder (N = 58)
	N (%)			
T. gondii levels				
Mean (SD)	2.03 (1.02)	2.04 (0.84)	1.92 (0.75)	2.11 (0.72)
T. gondii (binary)				
Low *T. gondii*	2961 (91.30)	123 (93.18)	103 (94.50)	54 (93.10)
Elevated *T. gondii*	282 (8.70)	9 (0.82)	6 (5.50)	4 (6.90)
Sex				
Male	1462 (45.08)	54 (40.91)	42 (38.53)	14 (24.14)
Female	1777 (54.79)	77 (58.33)	67 (61.47)	44 (75.86)
Missing	4 (0.12)	1 (0.76)	0 (0)	0 (0)
Age at *T. gondii* serology sample				
7 years	451 (13.91)	20 (15.15)	19 (17.43)	8 (13.79)
11 years	2332 (71.91)	100 (75.76)	67 (61.47)	40 (68.97)
15 years	460 (14.18)	12 (9.09)	23 (21.10)	10 (17.24)
Depression symptoms				
No	2726 (84.06)	95 (71.97)	71 (65.14)	30 (51.72)
Yes	286 (8.82)	28 (21.21)	28 (25.69)	25 (43.10)
Missing	231 (7.12)	9 (6.82)	10 (9.17)	3 (5.17)
Cat ownership during gestation				
No	2064 (63.64)	76 (57.58)	71 (65.14)	37 (63.79)
Yes	948 (29.23)	47 (35.61)	31 (28.44)	15 (25.86)
Missing	231 (7.12)	9 (6.82)	7 (6.42)	6 (10.34)
Cat ownership during childhood				
No	822 (25.35)	25 (18.94)	29 (26.61)	13 (22.41)
Yes	1180 (36.39)	52 (39.39)	37 (33.94)	22 (37.93)
Missing	1241 (38.27)	55 (41.67)	43 (39.45)	23 (39.66)
Maternal marital status				
Unmarried	500 (15.42)	30 (22.73)	27 (24.77)	19 (32.76)
Married	2537 (78.23)	93 (70.45)	75 (68.81)	33 (56.9)
Missing	206 (6.35)	9 (6.82)	7 (6.42)	6 (10.34)
Maternal SES				
Manual	2281 (70.34)	89 (67.42)	73 (66.97)	27 (46.55)
Non-manual	375 (11.56)	20 (15.15)	14 (12.84)	13 (22.41)
Missing	587 (18.10)	23 (17.42)	22 (20.18)	18 (31.03)
Maternal education				
A-levels or lower	2367 (72.99)	102 (77.27)	79 (72.48)	46 (79.31)
Degree or higher	637 (19.64)	21 (15.91)	23 (21.1)	8 (13.79)
Missing	239 (7.37)	9 (6.82)	7 (6.42)	4 (6.90)
Household crowding (gestation)				
Mean (SD)	0.59 (0.38)	0.66 (0.36)	0.65 (0.33)	0.75 (0.40)
Household crowding (childhood)				
Mean (SD)	0.73 (0.28)	0.75 (0.21)	0.76 (0.31)	0.83 (0.28)
Maternal age				
Mean (SD)	29.22 (4.49)	28.91 (5.35)	28.15 (5.26)	26.98 (4.84)

3. Results

3.1. Sample characteristics

Of the 15,645 ALSPAC participants, N = 6846 participants (43.8%) had exposure data on *T. gondii* (N = 4298 at age 11, N = 1803 at age 15, and N = 745 at age 7). Of these, 3542 (51.2%) also had data on PEs at age 18 (including N = 2539 serum *T. gondii* at age 11, N = 505 serum *T. gondii* at age 15, and N = 498 serum *T. gondii* at age 7). A flow chart of sample sizes is shown in Fig. 1. Demographic characteristics for the sample included in the current analyses and the sample excluded due to missing data are included in supplementary Table S.1. Demographic characteristics for the analysis sample by PE group are shown in Table 1, and by depression status in supplementary Table S.2. The proportion of male participants was lower in the analysis sample compared to the full sample (44.4% vs 49.1%). Cat ownership was higher in the analysis sample than in the full sample both during gestation (29.4% vs 25.7%) and during childhood (36.5% vs 29.4%). Rates of elevated *T. gondii* were higher in the analysis sample than in the full ALSPAC sample (8.5% vs 3.5%), as were rates of depression symptoms (10.4% vs 3.3%). The analytic sample did not differ greatly from the full ALSPAC sample on maternal demographic characteristics (marital status, SES, education, and age at birth of study child).

MRI and serum *T. gondii* data were available for 334 participants from two ALSPAC imaging studies (n = 229 participants without PEs, n = 35 with suspected PEs, n = 41 with definite PEs, and n = 29 with psychotic disorder). Sample characteristics for the MRI sample are shown in Table 2.

3.2. Serum T. gondii and psychiatric symptoms

3.2.1. Psychotic experiences

When using serum *T. gondii* as a continuous measure (Fig. 2), higher

Table 2
MRI sample characteristics.

	Serology data available (N = 334)	Serology data missing (N = 79)
	N (%)/mean (SD)	N (%)/mean (SD)
Antipsychotic medications		
No	330 (98.8)	77 (97.47)
Yes	4 (1.2)	2 (2.53)
Sex		
Male	134 (40.12)	29 (36.71)
Female	200 (59.88)	50 (63.29)
Psychotic experiences		
None	229 (68.56)	46 (58.23)
Suspected	35 (10.48)	14 (17.72)
Definite	41 (12.28)	11 (13.92)
Psychotic disorder	29 (8.68)	8 (10.13)
Total intracranial volume	1449.23 (145.27)	1431.22 (141.15)
Age at scan	21.28 (1.46)	20.54 (1.17)

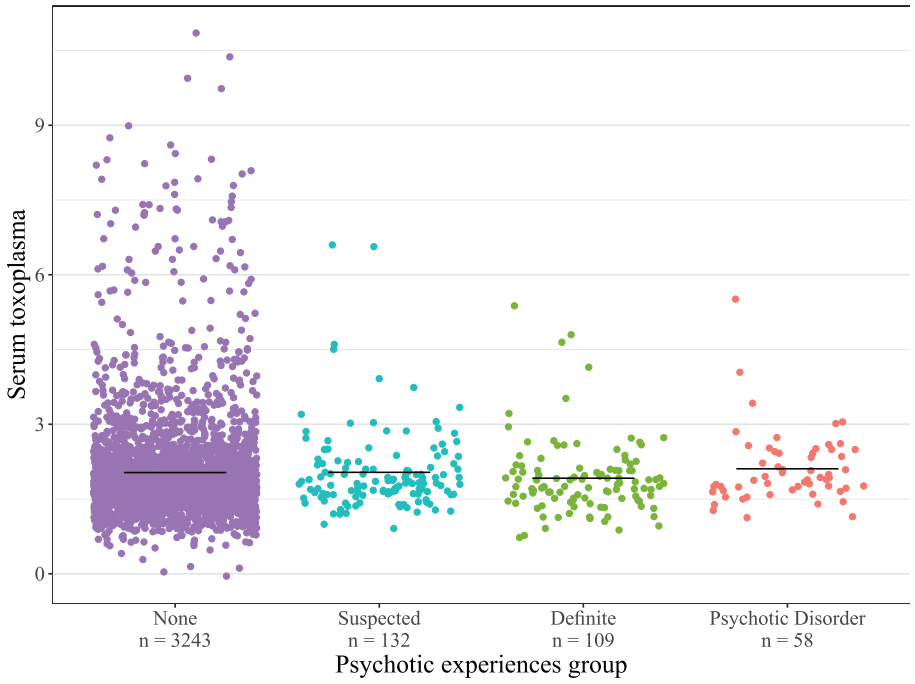

Fig. 2. Scatter plot of serum *T. gondii* at age 7, 11, or 15 by psychotic experiences group at age 18.

Table 3
Univariable and multivariable risk ratios (RRs) and 95% confidence intervals (CIs) for the associations between serum *T. gondii* and psychotic experiences (PEs) and between cat exposure (in gestation and in childhood) and PEs.

Exposure variable	PEs group	Unadjusted RR (95% CI)	*p*	Adjusted RR[a] (95% CI)	*p*
Serum *T. gondii*	Suspected PEs	1.00 (0.85–1.19)	0.959	1.06 (0.89–1.27)	0.492
	Definite PEs	0.87 (0.69–1.10)	0.244	0.86 (0.65–1.13)	0.269
	Psychotic disorder	1.07 (0.85–1.34)	0.574	1.00 (0.73–1.38)	0.996
Cat gestation	Suspected PEs	1.35 (0.93–1.95)	0.117	1.46 (0.98–2.16)	0.060
	Definite PEs	0.95 (0.62–1.46)	0.817	0.96 (0.60–1.55)	0.882
	Psychotic disorder	0.88 (0.48–1.62)	0.686	1.25 (0.64–2.45)	0.507
Cat childhood	Suspected PEs	1.45 (0.89–2.35)	0.134	1.66 (0.97–2.84)	0.064
	Definite PEs	0.89 (0.54–1.46)	0.640	0.80 (0.46–1.37)	0.415
	Psychotic disorder PEs	1.18 (0.59–2.35)	0.641	1.06 (0.47–2.38)	0.884

[a] Model adjusted for child's sex, age at serology sample collection, maternal marital status, maternal socioeconomic status, maternal education, maternal age at child's birth; reference category for risk ratios is no PEs.

serum concentrations were not associated with an increased risk of experiencing PEs (suspected PEs, definite PEs, psychotic disorder) in unadjusted or adjusted models (RRs = 0.86–1.06; *ps* ≥ 0.244) (Table 3). In sensitivity analyses, there was no evidence that participants who had elevated serum *T. gondii* (binary measure: ≥1 SD above sample mean vs. <1 SD above sample mean) had higher odds of experiencing any PEs (versus no PEs) in adulthood in unadjusted (OR = 0.71, 95% CI [0.43–1.12], *p* = 0.167) or adjusted models (OR = 0.81, 95% CI [0.46–1.34], *p* = 0.450).

3.2.2. Depression symptoms

Within the study sample, 3289 participants had depression data and serum *T. gondii* at age 11 (*N* = 2366), age 15 (*N* = 470), or age 7 (*N* = 453). Serum *T. gondii* as a continuous measure was not associated with depression in unadjusted (OR = 1.01, 95% CI [0.90–1.11], *p* = 0.923) or adjusted (OR = 0.97, 95% CI [0.85–1.10], *p* = 0.699) models (Fig. 3).

3.3. Cat ownership and psychotic experiences

There was weak evidence that risk of experiencing PEs in adulthood was associated with cat exposure during gestation (RRs 0.88–1.46, *ps* ≥ 0.060) or during childhood (RRs 0.80–1.45, *ps* ≥ 0.064) (Table 3).

3.4. Cat ownership and serum T. gondii

There was weak evidence that cat exposure during gestation was associated with higher serum *T. gondii* in adolescence in the unadjusted model (*mean difference* = 0.06, 95% CI [−0.003–0.14], *p* = 0.062). In the adjusted model, point estimates remained largely unchanged, albeit there was now stronger evidence of an association (*mean difference* = 0.08, 95% CI [0.01–0.16], *p* = 0.033) (Table 4). Cat ownership during childhood was not associated with increased serum *T. gondii* in adolescence in both unadjusted (*mean difference* = 0.06, 95% CI [−0.03–0.14], *p* = 0.193) and adjusted models (*mean difference* = 0.05, 95% CI [−0.04–0.14] *p* = 0.310). Household crowding did not moderate the association between *T. gondii* and cat exposure during gestation (*p-value for interaction* = 0.400) or during childhood (*p-value for interaction* = 0.325).

3.5. Serum T. gondii and grey matter volume

Voxel-wise whole-brain analyses revealed no significant associations between serum *T. gondii* and grey matter volume (*pFWEs* ≥ 0.882, *Zs* ≤ 3.86).

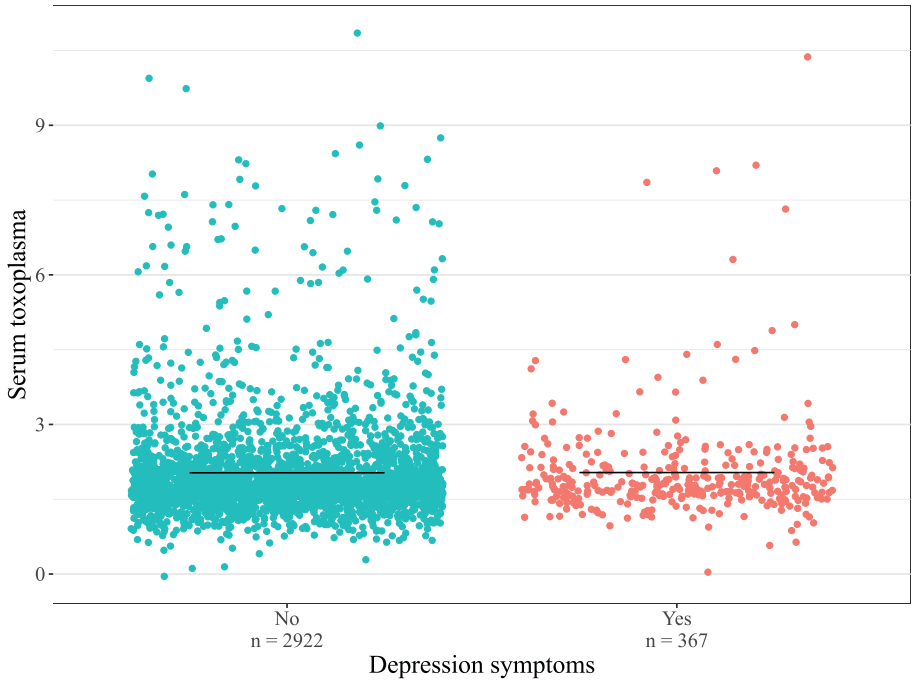

Fig. 3. Scatter plot of serum *T. gondii* at age 7, 11, or 15 by depression symptoms/diagnosis group at age 18.

Table 4
Results from univariable and multivariable linear regressions for the associations between cat exposure during gestation or childhood and serum *T. gondii*, with separate cat-ownership x household crowding interaction model.

Factor	Unadjusted	Adjusted [a]	Cat ownership * household crowding (interaction)[a]
Cat ownership during gestation	$\beta = 0.06$, *95% CI* [−0.003–0.14], $p = 0.062$	$\beta = 0.08$, *95% CI* [0.01–0.16], $p = 0.033$	$\beta = 0.12$, *95% CI* [−0.16–0.41], $p = 0.400$
Cat ownership during childhood	$\beta = 0.06$, *95% CI* [−0.03–0.14], $p = 0.193$	$\beta = 0.05$, *95% CI* [−0.04–0.14], $p = 0.310$	$\beta = -0.21$, *95% CI* [−0.62–0.21], $p = 0.325$

[a] Model adjusted for child's sex, age at serology sample collection, maternal marital status, maternal socioeconomic status, maternal education, maternal age at child's birth; household crowding was not included in the adjusted model and was only included in the interaction model.

4. Discussion

This study sought to investigate the association between serum levels of *T. gondii* in childhood and psychotic experiences (PEs) at age 18. The results suggest that *T. gondii* in childhood is not associated with an increased risk of developing PEs. There was no association between cat ownership during childhood and *T. gondii*, indicating that results from previous studies examining cat ownership during childhood as a proxy measure of *T. gondii* exposure may be overstated. Conversely, maternal cat ownership during gestation may be a suitable proxy measure for use by future studies, as this was associated with *T. gondii*, although prior studies have tended to focus exclusively on childhood exposure (McGrath et al., 2024). Consistent with the finding that *T. gondii* is not associated with PEs, *T. gondii* was not associated with changes in grey matter volume. *T. gondii* was also not associated with depression symptoms or diagnosis, in line with previous literature (Nayeri Chegeni et al., 2019).

The absence of an association between *T. gondii* and PEs reported here contrasts with prior research, which has demonstrated the presence of an association between *T. gondii* and increased risk of a schizophrenia diagnosis (McGrath et al., 2024). This discrepancy may suggest that the association exists only for schizophrenia, but not for sub-clinical levels of symptoms seen in those with PEs. Indeed, previous studies examining the association between cat exposure and psychotic-like experiences found no association, particularly in adjusted analyses (Kolpakova and Bedwell, 2013; Lindgren et al., 2018; Palomäki et al., 2019; Solmi et al., 2017), although some reported an association between psychotic-like experiences and being bitten by a cat (Kolpakova and Bedwell, 2013) and ownership of rodent-hunting cats (Paquin et al., 2022). However, our PE sample includes a sub-sample of participants with 'psychotic disorder', defined as those experiencing psychotic symptoms associated with distress or a decline in functioning or help seeking, although this group was smaller than the sub-clinical groups.

In our sample, the prevalence of elevated serum *T. gondii* (8.5%) and PEs ($N = 299$) was low, which limits power to detect small associations in the sensitivity analysis using *T. gondii* as a binary variable. The pooled unadjusted odds ratio reported in a prior meta-analysis examining toxoplasmosis and schizophrenia (Contopoulos-Ioannidis et al., 2022) was 1.91; our study has approximately 93% power to detect an effect of that size. However, effects for PEs are likely to be smaller than those observed for schizophrenia. Consistent with this, our study has approximately 80% power to detect an odds ratio of 1.72 for the association between elevated *T. gondii* and PEs (two-sided $\alpha = 0.05$). The prevalence of elevated *T. gondii* in our sample was consistent with other UK-based samples (Burrells et al., 2016), and the confidence intervals around our estimates were reasonably narrow. Together, our results suggest that large positive associations between *T. gondii* and PEs are unlikely, though smaller effects cannot be excluded. Notably, many prior studies examined *T. gondii* seropositivity, using heterogeneous cut-offs used for seropositivity that vary widely between studies (Contopoulos-Ioannidis et al., 2022; Fuller Torrey et al., 2007). To address this, the current study examined *T. gondii* both as a continuous and a binary measure of serum *T. gondii*, and neither was significantly associated with PEs.

A key strength of this study lies in its data being obtained prospectively, which reduces the risk of reverse causality or recall bias affecting

the findings. Another strength is the availability of blood samples for a large sample size, allowing serum *T. gondii* levels to be examined directly rather than relying on proxy measures such as cat ownership. This study also has several limitations which may impact the robustness of these findings. Due to the use of observational data, it is not possible to exclude the possibility of confounding affecting the results. However, this was partially mitigated by including sociodemographic factors known to be associated with psychosis risk, including maternal socioeconomic status, education, and age, as well as child's sex – in analyses examining the relationship between *T. gondii* and PEs. In addition, *T. gondii* serology and PE data are only available for a subset of the ALSPAC sample, which may introduce selection bias in the data. However, the analytic sample is similar to the full ALSPAC sample on most demographic variables. Some differences in depression or cat ownership rates are driven by differential missingness, as participants missing PEs or serology data were also more likely to have missing questionnaire data collected at the same assessment waves. Thus, missingness reflects observed variables (participation at a given wave), rather than underlying differences in participant characteristics.

We examined whether cat ownership is associated with *T. gondii* exposure; however, the timing of infection cannot be precisely determined. Serum *T. gondii* was measured during late childhood and therefore represents cumulative exposure up to the time of sampling, capturing infection acquired prenatally, in childhood, or later childhood. While this limits inference about when infection occurred, it does not preclude gestational exposure and represents a methodological improvement over studies relying solely on cat ownership as a proxy for exposure. Notably, gestational rather than childhood cat ownership showed the strongest association with serology in our data, although this finding is vulnerable to potential misclassification given the temporal gap. In addition, in analyses focusing on cat exposure as the exposure variable, individuals may have been misclassified for cat ownership if they initially did not have one at the earlier time point (8 months) and later acquired one but did not report so in the later questionnaires due to loss to follow-up or non-completion of those assessments. Furthermore, cat ownership was measured as a binary variable, which does not capture key features of exposure, including frequency of contact, indoor/outdoor cat status, or litter box handling, and therefore represents a crude proxy for potential *T. gondii* transmission.

In conclusion, elevated *T. gondii* levels in childhood are not associated with an increased risk of developing PEs or alterations in grey matter volume in adolescence. Moreover, only cat exposure during gestation, but not during childhood, is associated with *T. gondii* levels in childhood. Thus, future work examining the relationship between *T. gondii* and schizophrenia should focus on serology or mother's cat ownership during gestation as a proxy measure of *T. gondii* exposure, rather than childhood cat ownership.

CRediT authorship contribution statement

Jehanita Jesuthasan: Writing – review & editing, Writing – original draft, Methodology, Formal analysis, Conceptualization. **Kate Merritt:** Writing – review & editing, Methodology, Formal analysis, Conceptualization. **Francesca Solmi:** Writing – review & editing, Methodology. **Pedro Luque Laguna:** Writing – review & editing, Methodology. **Anthony S. David:** Writing – review & editing, Supervision, Methodology, Conceptualization.

Role of funding source

The funders played no role in the design of this study, the manuscript, or the decision to publish.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.schres.2026.01.022.

References

Boyd, A., Golding, J., Macleod, J., Lawlor, D.A., Fraser, A., Henderson, J., Molloy, L., Ness, A., Ring, S., Davey Smith, G., 2013. Cohort profile: the 'children of the 90s'—the index offspring of the Avon Longitudinal Study of Parents and Children. Int. J. Epidemiol. 42, 111–127. https://doi.org/10.1093/ije/dys064.

Burrells, A., Opsteegh, M., Pollock, K.G., Alexander, C.L., Chatterton, J., Evans, R., Walker, R., McKenzie, C.-A., Hill, D., Innes, E.A., Katzer, F., 2016. The prevalence and genotypic analysis of toxoplasma gondii from individuals in Scotland, 2006–2012. Paras. Vectors 9, 324. https://doi.org/10.1186/s13071-016-1610-6.

Contopoulos-Ioannidis, D.G., Gianniki, M., Ai-Nhi Truong, A., Montoya, J.G., 2022. Toxoplasmosis and schizophrenia: a systematic review and meta-analysis of prevalence and associations and future directions. PRCP 4, 48–60. https://doi.org/10.1176/appi.prcp.20210041.

Drakesmith, M., Caeyenberghs, K., Dutt, A., Zammit, S., Evans, C.J., Reichenberg, A., Lewis, G., David, A.S., Jones, D.K., 2015. Schizophrenia-like topological changes in the structural connectome of individuals with subclinical psychotic experiences. Hum. Brain Mapp. 36, 2629–2643. https://doi.org/10.1002/hbm.22796.

Drakesmith, M., Dutt, A., Fonville, L., Zammit, S., Reichenberg, A., Evans, C.J., Lewis, G., Jones, D.K., David, A.S., 2016a. Mediation of developmental risk factors for psychosis by white matter microstructure in young adults with psychotic experiences. JAMA Psychiatry 73, 396. https://doi.org/10.1001/jamapsychiatry.2015.3375.

Drakesmith, M., Dutt, A., Fonville, L., Zammit, S., Reichenberg, A., Evans, C.J., McGuire, P., Lewis, G., Jones, D.K., David, A.S., 2016b. Volumetric, relaxometric and diffusometric correlates of psychotic experiences in a non-clinical sample of young adults. NeuroImage Clin. 12, 550–558. https://doi.org/10.1016/j.nicl.2016.09.002.

Fonville, L., Cohen Kadosh, K., Drakesmith, M., Dutt, A., Zammit, S., Mollon, J., Reichenberg, A., Lewis, G., Jones, D.K., David, A.S., 2015. Psychotic experiences, working memory, and the developing brain: a multimodal neuroimaging study. Cereb. Cortex 25, 4828–4838. https://doi.org/10.1093/cercor/bhv181.

Fonville, L., Drakesmith, M., Zammit, S., Lewis, G., Jones, D.K., David, A.S., 2019. MRI indices of cortical development in young people with psychotic experiences: influence of genetic risk and persistence of symptoms. Schizophr. Bull. 45, 169–179. https://doi.org/10.1093/schbul/sbx195.

Fraser, A., Macdonald-Wallis, C., Tilling, K., Boyd, A., Golding, J., Davey Smith, G., Henderson, J., Macleod, J., Molloy, L., Ness, A., Ring, S., Nelson, S.M., Lawlor, D.A., 2013. Cohort profile: the Avon Longitudinal Study of Parents and Children: ALSPAC mothers cohort. Int. J. Epidemiol. 42, 97–110. https://doi.org/10.1093/ije/dys066.

Fuller Torrey, E., Bartko, J.J., Lun, Z.-R., Yolken, R.H., 2007. Antibodies to Toxoplasma gondii in patients with schizophrenia: a meta-analysis. Schizophr. Bull. 33, 729–736. https://doi.org/10.1093/schbul/sbl050.

Kolpakova, J., Bedwell, J.S., 2013. Childhood cat bites and disorganized symptoms of schizotypy in adulthood. Schizophr. Res. 146, 370–371. https://doi.org/10.1016/j.schres.2013.02.039.

Lancaster, T.M., Dimitriadis, S.L., Tansey, K.E., Perry, G., Ihssen, N., Jones, D.K., Singh, K.D., Holmans, P., Pocklington, A., Davey Smith, G., Zammit, S., Hall, J., O'Donovan, M.C., Owen, M.J., Linden, D.E., 2019. Structural and functional neuroimaging of polygenic risk for schizophrenia: a recall-by-genotype–based approach. Schizophr. Bull. 45, 405–414. https://doi.org/10.1093/schbul/sby037.

Lewis, G., Pelosi, A.J., Araya, R., Dunn, G., 1992. Measuring psychiatric disorder in the community: a standardized assessment for use by lay interviewers. Psychol. Med. 22, 465–486. https://doi.org/10.1017/S0033291700030415.

Lindgren, M., Torniainen-Holm, M., Härkänen, T., Dickerson, F., Yolken, R.H., Suvisaari, J., 2018. The association between toxoplasma and the psychosis continuum in a general population setting. Schizophr. Res. 193, 329–335. https://doi.org/10.1016/j.schres.2017.06.052.

Maisarah, A., Mohamad, S., Husain, M., Abdullah, S., Noordin, R., 2022. Association between infection with *Toxoplasma gondii* and psychiatric disorders. Folia Parasitol. 69. https://doi.org/10.14411/fp.2022.008.

McGrath, J.J., Lim, C.C.W., Saha, S., 2024. Cat ownership and schizophrenia-related disorders and psychotic-like experiences: a systematic review and meta-analysis. Schizophr. Bull. 50, 489–495. https://doi.org/10.1093/schbul/sbad168.

Mitchell, R.E., Jones, H.J., Yolken, R.H., Ford, G., Jones-Brando, L., Ring, S.M., Groom, A., FitzGibbon, S., Smith, G.D., Timpson, N.J., 2018. Longitudinal serological measures of common infection in the Avon Longitudinal Study of Parents and Children cohort. Wellcome Open Res. 3, 49. https://doi.org/10.12688/wellcomeopenres.14565.2.

Monroe, J.M., Buckley, P.F., Miller, B.J., 2015. Meta-analysis of anti-*Toxoplasma gondii* IgM antibodies in acute psychosis. SCHBUL 41, 989–998. https://doi.org/10.1093/schbul/sbu159.

Nayeri Chegeni, T., Sharif, M., Sarvi, S., Moosazadeh, M., Montazeri, M., Aghayan, S.A., Balalami, N.J., Gholami, S., Hosseininejad, Z., Saberi, R., Anvari, D., Gohardehi, S., Daryani, A., 2019. Is there any association between Toxoplasma gondii infection and depression? A systematic review and meta-analysis. PloS One 14, e0218524. https://doi.org/10.1371/journal.pone.0218524.

Niarchou, M., Zammit, S., Lewis, G., 2015. The Avon Longitudinal Study of Parents and Children (ALSPAC) birth cohort as a resource for studying psychopathology in childhood and adolescence: a summary of findings for depression and psychosis. Soc. Psychiatry Psychiatr. Epidemiol. 50, 1017–1027. https://doi.org/10.1007/s00127-015-1072-8.

Oncu-Oner, T., Can, S., 2022. Meta-analysis of the relationship between *Toxoplasma gondii* and schizophrenia. Ann. Parasitol. 68.

Palomäki, J., Koskela, J., Suvisaari, J., Yolken, R., Torrey, F., Veijola, J., 2019. Cat ownership in childhood and development of schizophrenia. Schizophr. Res. 206, 444–445. https://doi.org/10.1016/j.schres.2018.12.020.

Paquin, V., Elgbeili, G., Munden, J., Schmitz, N., Joober, R., Ciampi, A., King, S., 2022. Conditional associations between childhood cat ownership and psychotic experiences in adulthood: a retrospective study. J. Psychiatr. Res. 148, 197–203. https://doi.org/10.1016/j.jpsychires.2022.01.058.

Solmi, F., Hayes, J.F., Lewis, G., Kirkbride, J.B., 2017. Curiosity killed the cat: no evidence of an association between cat ownership and psychotic symptoms at ages 13 and 18 years in a UK general population cohort. Psychol. Med. 47, 1659–1667. https://doi.org/10.1017/S0033291717000125.

Sutterland, A.L., Mounir, D.A., Ribbens, J.J., Kuiper, B., Van Gool, T., De Haan, L., 2020. Toxoplasma gondii infection and clinical characteristics of patients with schizophrenia: a systematic review and meta-analysis. Schizophr. Bull. Open 1, sgaa042. https://doi.org/10.1093/schizbullopen/sgaa042.

Tenter, A.M., Heckeroth, A.R., Weiss, L.M., 2000. Toxoplasma gondii: from animals to humans. Int. J. Parasitol. 30, 1217–1258. https://doi.org/10.1016/S0020-7519(00)00124-7.

Torrey, E.F., 2022. The case for Toxoplasma gondii in psychosis and other human diseases. In: Parasites, Pussycats and Psychosis. Springer International Publishing, Cham, pp. 11–28. https://doi.org/10.1007/978-3-030-86811-6_2.

Webster, J.P., Kaushik, M., Bristow, G.C., McConkey, G.A., 2013. *Toxoplasma gondii* infection, from predation to schizophrenia: can animal behaviour help us understand human behaviour? J. Exp. Biol. 216, 99–112. https://doi.org/10.1242/jeb.074716.

World Health Organization, 1994. Schedules for Clinical Assessment in Neuropsychiatry: Version 2. American Psychiatric Press.

Zammit, S., Kounali, D., Cannon, M., David, A.S., Gunnell, D., Heron, J., Jones, P.B., Lewis, S., Sullivan, S., Wolke, D., Lewis, G., 2013. Psychotic experiences and psychotic disorders at age 18 in relation to psychotic experiences at age 12 in a longitudinal population-based cohort study. AJP 170, 742–750. https://doi.org/10.1176/appi.ajp.2013.12060768.

Zhu, Y., Yang, X., Chen, M., Hu, Y., Chang, Y., Wu, X., 2024. Research progress on the association between schizophrenia and toxoplasma gondii infection. Biomed. Environ. Sci. 37, 647–660.