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# Risky business: linking *Toxoplasma gondii* infection and entrepreneurship behaviours across individuals and countries

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Disciplines such as business and economics often rely on the assumption of rationality when explaining complex human behaviours. However, growing evidence suggests that behaviour may concurrently be influenced by infectious microorganisms. The protozoan *Toxoplasma gondii* infects an estimated 2 billion people worldwide and has been linked to behavioural alterations in humans and other vertebrates. Here we integrate primary data from college students and business professionals with national-level information on cultural attitudes towards business to test the hypothesis that *T. gondii* infection influences individual- as well as societal-scale entrepreneurship activities. Using a saliva-based assay, we found that students ($n = 1495$) who tested IgG positive for *T. gondii* exposure were 1.4× more likely to major in business and 1.7× more likely to have an emphasis in 'management and entrepreneurship' over other business-related emphases. Among professionals attending entrepreneurship events, *T. gondii*-positive individuals were 1.8× more likely to have started their own business compared with other attendees ($n = 197$). Finally, after synthesizing and combining country-level databases on *T. gondii* infection from the past 25 years with the Global Entrepreneurship Monitor of entrepreneurial activity, we found that infection prevalence was a consistent, positive predictor of entrepreneurial activity and intentions at the national scale, regardless of whether previously identified economic covariates were included. Nations with higher infection also had a lower fraction of respondents citing 'fear of failure' in inhibiting new business ventures. While correlational, these results highlight the linkage between parasitic infection and complex human behaviours, including those relevant to business, entrepreneurship and economic productivity.

## Significance statement

*Toxoplasma gondii* is a protozoan parasite estimated to infect over 2 billion people worldwide. While rarely associated with acute pathology, latent infections have increasingly been linked to subclinical outcomes such as car accidents, neuroticism and suicides through their potential influence on personality and risk-taking behaviours. Whether such effects extend to business-related behaviours among individuals and across populations remains conjectural. By combining data from university students, business professionals and global databases, we highlight the consistent and positive link between *T. gondii* exposure and entrepreneurial behaviour at both local and international scales. These findings emphasize the 'hidden' role of parasites as potential drivers of complex human behaviour and economic outcomes.

## 1. Introduction

When explaining complex human behaviours, disciplines such as business and economics often rely heavily on the assumption of rationality—that individuals consider the costs, benefits, risks and probabilities of a decision and then behave in a way to maximize their own outcomes [1]. Although research in behavioural economics has increasingly acknowledged and explored the factors that contribute to deviations from rationality, these often focus on standard cognitive biases [2,3]. Comparatively little research has addressed the influence of biological factors generally, and of infectious microorganisms in particular, on the cornerstone assumption of rational decision-making [4,5] and overall patterns of impulsivity, including risk-taking behaviour [6]. Emerging research in the biological sciences highlights the importance of transmissible agents—ranging from viruses to worms—in collectively shaping host immunity, mental health and even mate attraction [7–9]. The goal of this study was to investigate how infection by a globally distributed parasite—through its potential influence on individual human behaviour—is associated with local to large-scale cultural and business-related outcomes, specifically entrepreneurship.

The protozoan parasite *Toxoplasma gondii* infects an estimated 2 billion people worldwide [10,11]. Although over 100 species of vertebrates can become infected with *T. gondii*, the parasite reproduces sexually only within wild and domestic cats [11,12]. Thus, adaptations by the parasite that increase predation risk by cats should be selectively favoured from an evolutionary standpoint [9,12,13]. Experimental studies from non-human systems indicate that *T. gondii* infection is associated with increased risk-taking behaviours, including an attraction towards cat urine, greater exploration of novel areas in mazes and reduced avoidance of open spaces [14–16]. Similar forms of both subtle and dramatic behavioural modification have been hypothesized in humans [17]: *T. gondii* has been linked to outcomes such as a greater risk of car accidents, mental illness, neuroticism, drug abuse and suicide [13,18–21]. The infection-associated changes in the brain that precipitate increased impulsivity are complex and not fully understood [22] although changes in the production, metabolism, or synthesis of both hormones (e.g. testosterone) and neurotransmitters (e.g. serotonin, dopamine and norepinephrine) have been explored [23]. Increases in testosterone, for instance, which have been linked to *T. gondii* infection [24], can enhance risk-taking behaviour, aggression and impulsivity in humans [17,25].

The psycho-behavioural linkages between *T. gondii* and human behaviour raise an intriguing question: to what extent do the effects of infection on behaviour affect individual- and population-level patterns in the success of new business ventures. Infection and the associated hormonal and neurological changes have the potential to amplify impulsivity, sensation-seeking, and risk-taking behaviours, as well as an individual's focus on ego, ambition, material possessions and self-achievement (at least in men)—characteristics often associated with entrepreneurial activity [17,20,26]. Studies of entrepreneurship at both the individual and societal levels have repeatedly emphasized the importance of specific traits, such as risk tolerance and lower fear of failure in determining entrepreneurship outcomes [27]. Alongside its effects on individuals, *T. gondii* infection has also been hypothesized to affect national-level cultural and economic outcomes [13,28]. There is strong global variation in *T. gondii* prevalence—from 9% in Norway to 60% in Brazil—which correlates positively with aggregate neuroticism [13] and negatively with institutional quality and economic performance by country [28].

Here we examined how infection by *Toxoplasma gondii* underlies heterogeneity in entrepreneurship attitudes and activity, first among individuals in university and professional populations, and then extending these results to global patterns in entrepreneurship. Specifically, we evaluate whether infection—through its hypothesized link to risk-taking behaviour—reduces the 'fear of failure' that often limits the entrepreneurial tendencies of individuals, thereby shaping larger-scale entrepreneurship activity and culture. Using a saliva-based assay of IgG antibodies, we tested the degree to which infection status predicted university students' tendency to major in business- and entrepreneurship-related disciplines, and professionals' success at starting their own business. To assess whether such individual-level patterns translated into national-scale outcomes, we coupled country-level databases on *T. gondii* infection from the past 25 years with results from the Global Entrepreneurship Monitor (GEM) of entrepreneurial activity, both with and without relevant covariates. By identifying how *T. gondii* infection at multiple scales predicts entrepreneurial activity and intent, these findings highlight the potential role of infectious organisms in shaping patterns of entrepreneurship behaviour and, by extension, the global economy.

## 2. Material and methods

### (a) Study 1: infection patterns in university students

Data on major field of study and *T. gondii* antibody prevalence were collected from 1495 undergraduate students in general biology and business classes at a large US university. Students apply for admission to one of the colleges on campus which include Arts and Sciences, Business, and Engineering. Once admitted to a college, students select a major emphasis of study within that college. Within Business, students can major in finance, accounting, marketing or management and entrepreneurship. Within Arts and Sciences, students can major in biology, psychology, physics, chemistry, among others.

While past research has often used serum samples, recent advances have facilitated the use of saliva as a less-invasive alternative to assess *T. gondii* infection [29]. Here, we used and validated an indirect competition immunoenzymatic (ELISA) saliva-based assay to test for *T. gondii* IgG antibodies. Subjects chewed on a sponge (Salivettes™) for 120 s, after which each sample was run in duplicate alongside five manufacturer IgG seropositive controls (provided by Accurun® 135), three saliva-positive controls (from known *T. gondii*-positive subjects), five saliva negative controls (from known *T. gondii*-negative subjects) and five blanks (samples with no saliva to baseline-correct the optical density (OD) per plate). Positive and negative saliva controls were tested using a quantitative immunoenzymatic assay for *Toxoplasma* IgG (Immuno-Biological Laboratory (IBL); Hamburg, Germany) and verified through a secondary reference laboratory (Quest Diagnostics™; San Juan, California) using a sandwich competitive ELISA. Subject samples were considered positive if the observed OD values were at least two standard deviations greater than the average negative control value from the corresponding plate. We validated this classification approach by calculating method sensitivity and specificity, as

well as comparisons with receiver operator characteristic curves based on threshold values (see electronic supplementary material, SI [30]). Ambiguous subjects in which the duplicate samples gave conflicting results were re-run. Results from antibody testing were linked to each student's indicated major, for which we performed comparisons both between Business-related majors and non-Business majors as well as within business-related majors by comparing the 'management and entrepreneurship' emphasis with all other business emphases (accounting, finance, marketing) and specifically to accounting, which is considered the most risk-avoidant emphasis considering its high placement rate (percent of students who receive job offers in their selected career field). Our rationale was that Business majors would be more interested in entrepreneurship than other majors and within the Business major, students who study 'management and entrepreneurship' would be more inclined towards entrepreneurship than other emphases, such as accounting. The total sample size of subjects with useable information on infection status and field of study was 1293 (electronic supplementary material, table S1).

### (b) Study 2: infection patterns in business professionals

To understand patterns of infection among professional entrepreneurs, we collected data from 197 individuals attending entrepreneurship events. All individuals at the locations were invited to participate by providing a saliva sample, as outlined above. Participants were given a colour-coded vial based on their sex and whether or not they had ever started their own company, and samples were processed as described above. For both Study 1 and Study 2, we used generalized linear models with a binomially distributed response and the complementary log–log link function to evaluate the influence of *T. gondii* infection status (antibody-negative versus antibody-positive) on major field of study (Business major versus non-Business majors, and 'management and entrepreneurship' emphasis versus other emphases within the Business discipline), and entrepreneurial tendencies (self-identified as having successfully started a business). Subject sex (male or female) and a sex-by-infection interaction were also included in all analyses; for Study 1, we also included a variable for grade point average (GPA) to account for grade-based admission requirements in different colleges (missing values were replaced with the mean GPA).

### (c) Study 3: global patterns of toxoplasmosis and entrepreneurship

Existing databases of *T. gondii* infection prevalence at the country level (the proportion of samples that tested positive for *T. gondii* within a country-specific survey) were compiled using published data and reviews (see electronic supplementary material). The data were restricted to studies conducted after 1990. When more than one *T. gondii* prevalence study was available for a given country, we used the average (electronic supplementary material, table S2). Because countries vary in the average age at which women get pregnant and thus the number of years of potential exposure to *T. gondii*, we used prevalence estimates standardized to an age of 22 years following Lafferty [13] (also see [28]).

To assess entrepreneurship, we used the GEM of entrepreneurial activity. The GEM database is the result of a worldwide consortium of universities (www.gemconsortium.org), with data derived from national surveys of entrepreneurial climate, activities and attitudes. We used GEM data collected from 2000 to 2010, using the most recent data for counties that were surveyed more than once during the study period. Our three dependent variables were the proportion of people in a country with entrepreneurial intentions (*Futsupno*), the proportion engaged in entrepreneurial activity (*teayy*), and the proportion inhibited from starting a business by their fear of failure (*Frfailop*) (see electronic supplementary material for additional variable descriptions). Because all dependent variables have values that range from zero to one, we used generalized linear models with a binomial distribution, following McDowell & Cox [31]. The control variables used in the standard GEM model [32] are described in the electronic supplementary material, although we ran analyses with and without these variables to ensure that findings were robust (see electronic supplementary material). Overlaying the GEM and *T. gondii* data sources yielded a database for 42 countries (see electronic supplementary material, table S2). We hypothesized that *T. gondii* prevalence would associate positively with the proportion of people in a given country that intend to start a new business or are currently engaged in entrepreneurial activities, and negatively with the proportion of people inhibited from starting a business by fear of failure. We did not include interactions between infection prevalence and GEM covariates given the lack of *a priori* hypotheses and the desire to avoid overfitting the models.

## 3. Results

### (a) Study 1: infection patterns in university students

Based on an analysis of *T. gondii* IgG prevalence from 1495 university students, 22% tested positive. There were 968 confirmed negative cases and 199 samples classified as 'ambiguous' even after retesting, which were removed from further analysis, leaving 1293 included cases. Using the 2SD classification method, 195 of 201 known positive samples (97% sensitivity) and 186 of 186 known negative samples (100% specificity) were classified correctly. Infection status was a significant, positive predictor of students' tendency to major in business-related fields ($B = 0.33$, s.e. $= 0.10$, $p < 0.005$), while controlling for sex and GPA (although results were comparable with these covariates removed). Among Business students, 146 of 475 individuals (31%) tested positive for *T. gondii* IgG, whereas 179 of 818 (22%) of non-Business majors were antibody-positive. The odds of being a Business major were 1.4× greater for antibody-positive students [95% CI = (1.1, 1.7)] relative to those testing negative (figure 1). Female students were also less likely to be Business majors ($B = -0.53$, s.e. $=$ 0.09, $p < 0.01$), whereas GPA had no effect. Within the Business major specifically, students with evidence of *T. gondii* exposure were 1.7× more likely to have an established emphasis in 'management and entrepreneurship' [95% CI = (1.0, 2.8)] relative to other Business subdisciplines ($B = 0.52$, s.e. $= 0.27$, $p = 0.054$ (figure 1). Twenty-four of the 57 (42%) 'management and entrepreneurship' majors tested positive for *T. gondii* compared with 63 of the 216 (29%) students majoring in accounting, finance or marketing. GPA also associated negatively with the management/entrepreneurship emphasis ($B = -0.68$, s.e. $= 0.29$, $p < 0.05$), while sex showed no relationship. This contrast was even more pronounced in comparing the influence of infection status on the likelihood of a concentration in management/entrepreneurship versus accounting specifically ($B = 0.63$, s.e. $=$ 0.30, $p < 0.05$). There were no significant interactions between sex and infection status for any of the response variables, and statistics are reported from models without this term.

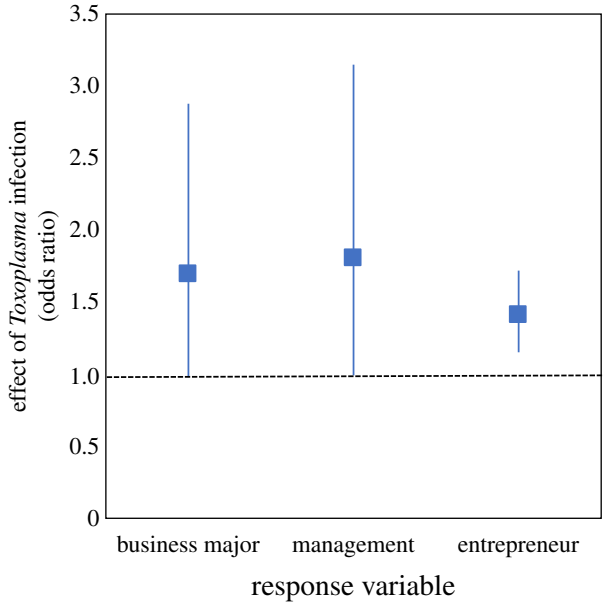


**Figure 1.** Relation between *T. gondii* infection and entrepreneurial outcomes among university students and business professionals. Presented for each analysis is the odds ratio (±0.95% CI) for infection on: the likelihood a sampled student was a Business major relative to an Arts and Sciences major ($n = 1293$), whether Business majors self-selected into the management and entrepreneurship focus relative to other business-related subdisciplines ($n = 273$), and, among professionals in the community, the likelihood an individual successfully started a business ($n = 197$). For the analyses of student majors, GPA, and sex were included as covariates; for the professionals, sex was included as a covariate. (Online version in colour.)

### (b) Study 2: infection patterns in entrepreneurs

Consistent with the undergraduate data, *T. gondii* antibody status was a positive predictor of entrepreneurship among professionals attending entrepreneurship events ($B = 0.59$, s.e. $= 0.29$, $p < 0.05$). The odds of having successfully started a business were 1.8× greater among antibody-positive individuals [95% CI = (1.0, 3.2)] compared with those who tested negative (4 of 73 versus 17 out of 124) (figure 1).

### (c) Study 3: global patterns of toxoplasmosis and entrepreneurship

Extending the analysis of infection and entrepreneurship to the global extent, we detected a positive association between *T. gondii* infection prevalence among 42 countries and both the proportion of people intending to start their own business ($B = 2.49$, s.e. $= 0.30$, $p < 0.001$; figure 2*a*) and the proportion currently engaged in entrepreneurial activity ($B = 1.39$, s.e. $= 0.38$, $p < 0.01$; figure 2*b*) (see electronic supplementary material, tables S3 and S4). Correspondingly, *T. gondii* infection negatively predicted the proportion of a country's population inhibited from starting a business by their fear of failure ($B = -0.71$, s.e. $= 0.24$, $p < 0.01$; figure 2*c*). Among all countries, the average age-adjusted *T. gondii* prevalence was 0.34 (figure 2). The heat map shows countries with greater levels of entrepreneurship (darker blue countries) have higher *T. gondii* prevalence (darker red dots). These results were robust to alternative forms of analysis and the inclusion of standard control covariates (see electronic supplementary material). Thus, the coefficient estimates for *T. gondii* prevalence on each entrepreneurship response variable were broadly consistent regardless of whether covariates from the GEM model were included (figure 3).

## 4. Discussion

Research in business and economics have traditionally emphasized the importance of rationality in explaining complex human behaviours [33], yet the additional influence of biological factors generally and of infectious microorganisms in particular on this cornerstone assumption have rarely been examined [4,5]. By integrating research on entrepreneurship, epidemiology, and behavioural outcomes, this study highlights linkages between infection by the globally distributed parasite *T. gondii* and entrepreneurship behaviours among individuals and across countries. Based on a saliva-based antibody assay applied to 1495 students from a large US university, infection increased the odds of majoring in a Business-related discipline by 1.4× relative to uninfected students. Within Business majors specifically, *T. gondii*-positive individuals were 1.7× more likely to have self-selected into the 'management and entrepreneurship' emphasis relative to other emphases (accounting, finance and marketing). Extending this analysis to members of the professional community, Study 2 indicated that individuals previously exposed to *T. gondii* were 1.8× more likely to have started a business relative to attendees who tested negative. By combining global information on *T. gondii* prevalence and entrepreneurship behaviours among 42 countries, our analyses further indicated that populations with higher *T. gondii* prevalence had greater intentions to start a business and higher levels of active entrepreneurship behaviours. These countries also had a lower fraction of respondents who cited 'fear of failure' as a factor preventing them from initiating a business-related enterprise.

Mechanistically, the observed linkages between *T. gondii* infection and entrepreneurship among students, professionals, and nations have several potential interpretations. Given the correlational nature of the study, observed patterns may not be causal; for example, higher risk-takers could be more likely to be both entrepreneurial and exposed to *T. gondii* (e.g. by consuming raw/undercooked meat), thereby driving the correlation. Although causality cannot be inferred, the cross-sectional field design represents a strength of the current study in comparison to case-control methodology, for which the selection of controls is non-random and influenced by self-selection biases [34]. By surveying a population of students, rather than known-positives and matched controls, we minimized the risk of selection bias in that regard. Nonetheless, whether an individual becomes an entrepreneur depends on many factors, such as access to resources and institutional support (e.g. [35]). Thus, the relationship between *T. gondii* and a complex phenomenon such as entrepreneurial activity is expected to be multifactorial and probably influenced by additional, unmeasured variables that affect both parasite exposure and entrepreneurship at the individual or national scale. At the global extent, for instance, patterns related to climate, ecology, soil exposure or biogeographic history probably affect the distribution of parasite exposure directly or through their influence on food preferences (including the consumption of raw or undercooked meat) and human culture [11,36–38].

The more intriguing possibility is that infection directly or indirectly enhances entrepreneurial tendencies within individuals and specific cultures. Experimental evidence

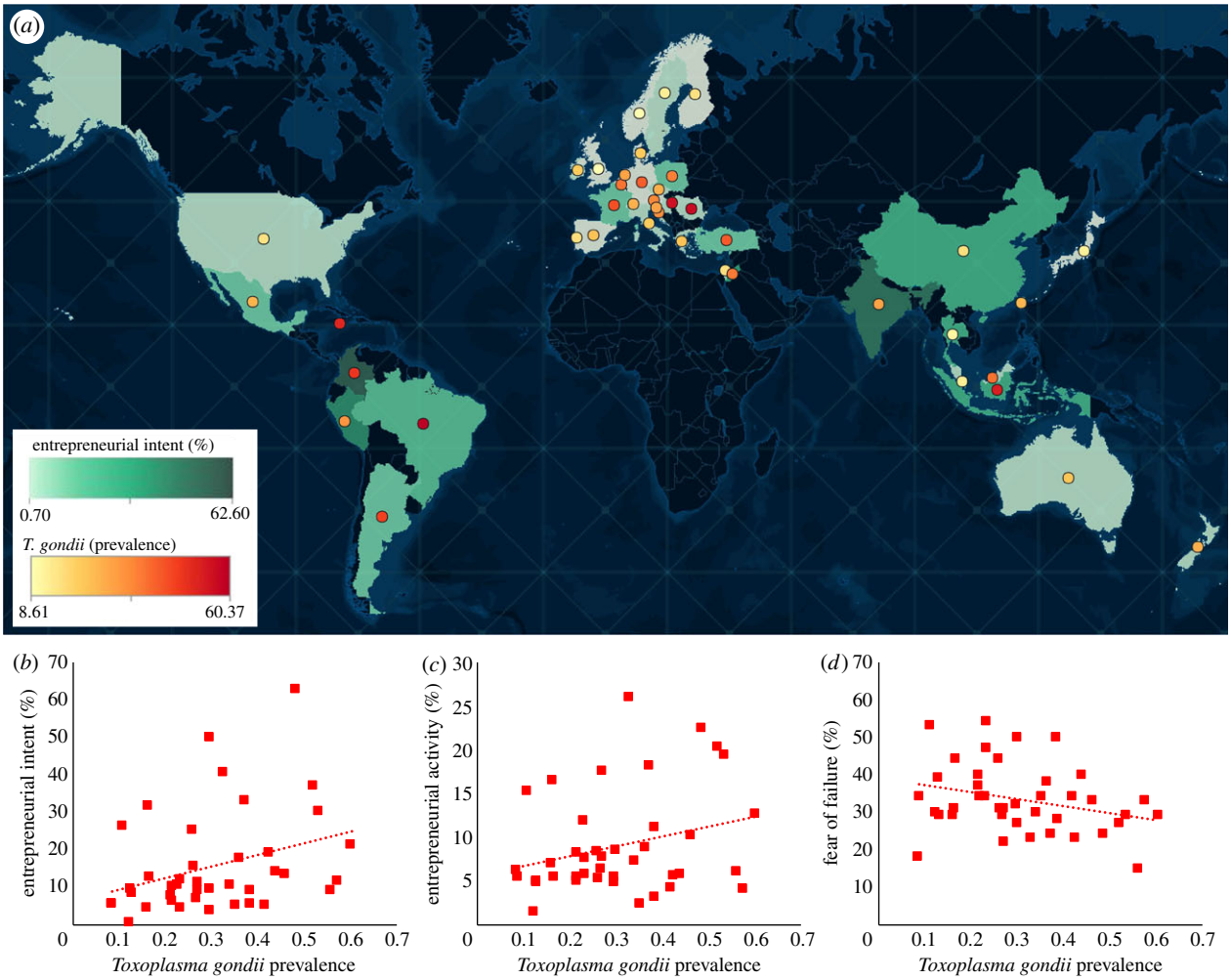


**Figure 2.** Heat map illustrating the geographical distribution of *T. gondii* infection and the proportion of a country's population with entrepreneurial intentions. (*a*) The colour of the country reflects the fraction of surveyed respondents with intentions to start their own business (from light blue to dark blue), while the colour of the superimposed circle reflects the magnitude of infection (from light yellow to dark red). Only countries with surveys of *T. gondii* and entrepreneurial activity since 1990 are included. Infection data from Maseland [28] and sources therein while entrepreneurship information was derived from the GEM database. The relationship between *T. gondii* infection prevalence and the three specific variables related to entrepreneurial attitudes and activity are presented in the scatterplots. Response variables from the GEM database included the proportion of a country's population (*b*) with entrepreneurial intentions (intend to start a business within three years), (*c*) that are currently engaged in entrepreneurial activity, or (*d*) that cited 'fear of failure' as a factor inhibiting them from starting a business. All relationships were significant based on generalized linear models with a binomial distribution (see electronic supplementary material, tables S2, S3 and S4). (Online version in colour.)

from rodent models is often cited to support the causal link between infection and altered host behaviour [39–41]. Infection is associated with increased risk-taking behaviours, potentially due to hormonal or neurological changes resulting from encysted *T. gondii* in the brain [42]. Samojlowicz *et al*. [21] found a significant, positive relationship between *T. gondii* infection and risky behaviours, including substance overdose, suicide, not wearing a helmet and alcohol consumption. Correspondingly, entrepreneurs tend to score higher in risk-taking (and lower in risk-avoidance), need for achievement and overconfidence [43]. The hypothesized increase in impulsivity and risk-taking associated with infection could, therefore, encourage individuals to engage in entrepreneurial activity [17,21]. Although this study did not include specific measures of personality, individual infection status among university students and business professionals was a positive predictor of interest in entrepreneurship or entrepreneurial success. Among nations, higher levels of infection were associated with a reduction in the population's 'fear of failure' in initiating a business venture, consistent with higher overall levels of entrepreneurial intent or activity (figure 2). This relationship persisted even when controlling for previously identified covariates from the GEM database, such as financial need, institutional or governmental support, educational opportunities and social norms (electronic supplementary material; figure 3). Previous analysis of the GEM database shows that factors like social norms and education are among the most highly related factors to entrepreneurship [28].

Previous, large-scale analyses of *T. gondii* prevalence among countries have shown that infection is linked to neuroticism, uncertainty avoidance, and economic prosperity [13,28]. For example, Lafferty [13] found that infection prevalence among 27 Western nations correlated negatively with uncertainty avoidance, although this relationship was not significant when eastern and Western cultures were combined. Maseland [28] reported a negative link between *T. gondii* infection and the economic outcomes of associated nations, including the countries used here. Arguably, such findings might lead to the opposite expectation of the patterns observed in the current study: that infection prevalence would associate with more risk-averse individuals and

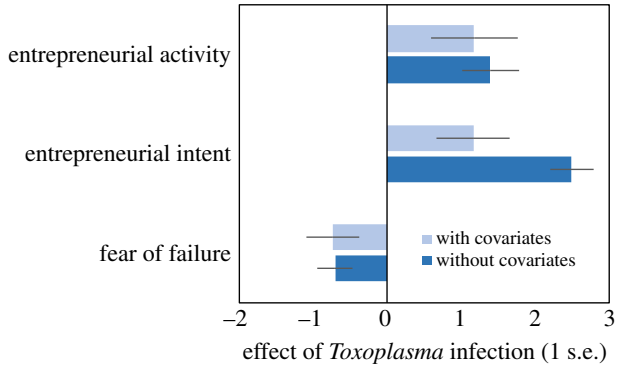


**Figure 3.** Coefficient estimates (± 1 s.e.) for *T. gondii* infection prevalence on entrepreneur-related responses from the GEM database, both with and without standard covariates from previous analyses [25]. Estimates are derived from binomial models composed of data from 42 countries over the past 25 years. Overall, inclusion of covariates led to few changes in the estimates of *T. gondii*-associated effect sizes (see electronic supplementary material). (Online version in colour.)

reduced entrepreneurial innovation. However, extensive evidence linking infection to reduced fear makes a compelling case for a positive linkage with entrepreneurship [6,17]. The complex associations between *T. gondii* and behavioural patterns among countries may also depend on geographical variation in the strain or lineage of the parasite and the relative frequency of alternative exposure pathways (e.g. through cat exposure versus undercooked meat [10,11,44,45]).

The current findings raise questions regarding the implications of infection for individual entrepreneurs, aggregate societies and the associated economic outcomes. Entrepreneurship has been characterized as a high-risk, high-reward endeavour, for which the risk often comes at the cost of economic stability for an individual [46,47]. Because the risk almost always outweighs the reward, such that the probability of high reward is generally low, economic models indicate that entrepreneurship is rarely a rational decision for the individual [47]. Any factor that increases the tendency of an individual to engage in entrepreneurial activities would, therefore, amplify the probability of negative financial outcomes, except among the very poor for whom opportunity costs are lowest [46,47]. Among individuals who have already elected to become entrepreneurs, the potential effects of *T. gondii* on individual-based outcomes will depend on whether infection leads to poor decisions or simply limits the 'fear of failure' that would have otherwise impeded an entrepreneur from engaging in a successful endeavour. As we found in the global patterns study, reduced fear of failure could explain the relationship between *T. gondii* infection and entrepreneurship, although assessing this possibility will require comparisons of entrepreneurs as a function of *T. gondii* exposure history. By contrast with the consequences for individuals, there are clear benefits of increased entrepreneurship at the societal scale in terms of job growth, economic development, and innovation [48–51]; even if associated with greater infection by *T. gondii*, the enhanced innovation emerging from greater entrepreneurial engagement within the population would likely be positive. While increased disease risk is often associated with higher collectivism and greater xenophobia [52], its implications for transformational creativity and the resultant economic rewards remain relatively unexplored—particularly for pathogens that may cause individuals to deviate from rational economic theory.

In sum, emerging research in the biological sciences has increasingly emphasized the importance of transmissible agents—ranging from viruses to worms—in collectively shaping host immunity, mental health and even mate attraction [7–9]. Such findings suggest that infections—through their influence on individual behaviour—further have the potential to affect large-scale cultural and business-related outcomes. Here we hypothesized a connection between the general effects of *T. gondii* in individuals with extant entrepreneurship research, highlighting the alignment between psychological factors known to favour entrepreneurial intention and infection. What drives differences in entrepreneurial activity rates remains an important question (e.g. [53,54]), for which this study offers insight into the potential role of infection at the individual as well as country level (e.g. [55]).

Ethics. The data collection from humans was approved by the institutional review board at the University of Colorado (IRB Protocol no. 15-0004) and an informed consent form was given to all participants.

Data accessibility. The data and metadata associated with this article are available at Dryad Digital Repository (doi:10.5061/dryad.gd19rr3) [56].

Authors' contributions. S.K.J. and P.T.J.J. designed the study, all authors conducted the research, D.M.C. processed samples, M.A.F. and D.A.L. analysed country-level data, S.K.J. analysed individual-level data and wrote the first draft; all authors contributed to the final version of the manuscript.

Competing interests. We have no competing interests.

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