Induction of changes in human behaviour by the parasitic protozoan *Toxoplasma gondii*

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SUMMARY

Toxoplasma gondii, the coccidian parasite, is known to induce changes in the behaviour of its intermediate hosts. The high prevalence of this parasite in the human population (20–80%) offers the opportunity of studying the influence of the parasite on human behaviour by screening of a normal population. A total of 224 men and 170 women were tested for toxoplasmosis and their personality profiles were measured by Cattell's questionnaire. Highly significant differences between *Toxoplasma*-infected and uninfected subjects were observed ($P < 0{\cdot}01$). For men the factors *G* (low superego strength), *L* (protension), *O* (guilt proneness), and *Q2* (group dependency) were positively influenced in infected subjects. For women the prevailing factors were *A* (affectothymia, $P < 0{\cdot}01$), *L* (alaxia), *O* (untroubled adequacy) and *Q2* (self-sufficiency). To reveal whether toxoplasmosis induces personality factor-shifts or whether certain combinations of personality factors influence the probability of acquiring *Toxoplasma* infection, we examined the personality profiles of 164 male patients diagnosed with acute toxoplasmosis during the past 13 years. The existence of a positive correlation between the duration of latent toxoplasmosis and the intensity of superego strength decrease ($P < 0{\cdot}02$) suggested that the decrease of superego strength (the willingness to accept group moral standards) was induced by *T. gondii* infection.

Key words: *Toxoplasma*, behaviour, manipulation hypothesis, personality, Cattell's questionnaire.

INTRODUCTION

The ability of parasites to manipulate host behaviour has been observed in many animal models (Barnard & Behnke, 1990). Parasites with complicated life-cycles often induce changes in the behaviour of their intermediate hosts that increase the susceptibility of a parasitized animal to predation. Among parasitic protozoa from the Sarcocystidae Poche, 1913, the phenomenon has been observed in *Sarcocystis–Microtus* (Hoogenboom & Dijkstra, 1987), *Sarcocystis–Dicrostonyx*, (Quinn, Brooks & Cawthron, 1987), *Toxoplasma–Rattus* (Webster, 1994; Webster *et al.* 1994), *Toxoplasma–Mus* (Arnott *et al.* 1990; Hay, Aitken & Arnott, 1985; Hay *et al.* 1983; Hutchison *et al.* 1980*a*, *b*) parasite–host systems. The last parasite, *Toxoplasma gondii*, is an intestinal coccidian of felids with an unusually wide range of intermediate hosts, including humans. After an acute phase of infection (promoted by tachyzoites), pseudocysts are formed mainly in the neural and muscular tissues of infected hosts. The parasites (bradyzoites) cause little or no harm to immunocompetent individuals while inside the cysts and probably persist as viable parasites for the life-span of the host (Remington & Krahenbuhl, 1982).

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Transmission of *T. gondii* from the intermediate to the definitive host is by carnivorism. Since sexual reproduction of *T. gondii* can be accomplished only in cats, strong selection pressure on *Toxoplasma* exists to evolve a mechanism of manipulating intermediate host behaviour.

The high incidence of latent toxoplasmosis (the presence of anti-*Toxoplasma* immunity in human subjects without any clinical symptoms of acute disease) in different countries (about 22% of pregnant women in London, 32% in New York City, and 84% in Paris (Desmonts & Couvreul, 1974)) offers the opportunity to study the possible influence of latent toxoplasmosis on human behaviour.

This study is concerned with the effect of latent *T. gondii* infection on human behaviour and involves the comparison of 394 personality profiles of health subjects. The causality of the observed association of personality factor-shift and latent toxoplasmosis is studied by searching for a positive correlation between the extent of the shift and the duration of latent toxoplasmosis on another experimental set of 164 men diagnosed with acute toxoplasmosis during the past 13 years.

MATERIALS AND METHODS

Subjects

Data were collected over a period of 26 months in 1992–1994. The first experimental set (Biologists)

was composed of 224 men and 170 women, mostly staff and biology students of zoology departments of the Faculty of Science, Charles University, Prague. The second set (patients) contained 190 men diagnosed with acute toxoplasmosis during the past 13 years in various Prague hospitals. All subjects gave their informed consent before they were accepted for the study.

Personality tests

Cattell's 16-factor questionnaire (form A) (Cattell, 1970) was used for the characterization of personalities. This questionnaire is widely used for personality studies in many countries, including the Czech Republic (Christiansen *et al.* 1994; Grossman & Craig, 1995). It covers 16 personality factors (Table 1). The main advantage of this traditional test is that it contains only 187 questions. Therefore, it can be completed by most subjects within 1 h. In the first experimental set all subjects (except 22 parasitologists) completed their questionnaires before the results of the toxoplasmosis test were known. In the second set the subjects obtained the questionnaire by mail. In the enclosed letter they were informed about the general aim of the research (a study of the influence of toxoplasmosis on human personality) and were asked to participate in the project. No differences between the sets of responders (190) and non-responders (360) were observed in age, length of infection, occupation or any other characteristic compared.

Immunological tests for toxoplasmosis

The existence of specific immunity was assessed by an intradermal delayed hypersensitivity test (IDHT) (Feldman, 1954). This test yields presence/absence data. The test was performed using Toxoplasmin (SEVAC, USOL, Prague) as the antigen and sham injection of pure solution as negative control. Positive reactions were of the delayed tuberculin type and were measured 48 h after antigen administration. The large-scale use of the skin test in population surveys has shown excellent correlation between the results of this test and the presence or absence of humoral antibodies (Remington & Krahenbuhl, 1982). The ability to elicit delayed hypersensitivity to *Toxoplasma* antigens in man may require a period of months or even years after initial infection to develop and usually lasts for the rest of the host's life, so it is the best method for the diagnosis of latent infection (Remington & Krahenbuhl, 1982).

The serological data and the addresses of patients with acute toxoplasmosis were obtained from the database of patients at the National Diagnostic Laboratory for Toxoplasmosis, National Institute of Public Health, Prague, Czech Republic. Acute toxoplasmosis was diagnosed on the basis of clinical symptoms and results of different serological tests, including indirect fluorescent antibody test, IFAT, (Goldman, 1957), complement-fixation test, CFT, (Warren & Sabin, 1942), and IgG and IgM ELISA (Pokorný *et al.* 1989, 1990).

Statistics

The raw data (age- non-standardized) from the questionnaire were used in statistical analysis to prevent information loss during the transformation of 27-point raw scales into 10-point age-standardized scales and to avoid an application of general population-based correction factors on the 'non-standard' subpopulation of biologists. The effect of age was controlled either by using residuals of regression between age and the raw personality factors, or by using multidimensional statistical methods with the age of a person as a covariate.

The Statistica® program was used for all statistical testing. A multivariate analysis of covariance MANCOVA was used to study the effects of toxoplasmosis, gender and toxoplasmosis–gender interactions on personality factors. Discriminant function analysis was used for personality factor-based diagnosis of toxoplasmosis and logistic regression or discriminant function analysis for estimation of specific effects of toxoplasmosis on particular personality factors. A multiple linear regression was used to estimate the correlation between the length of latent toxoplasmosis and the extent of personality factor-shift.

RESULTS

Difference between Toxoplasma-*infected and* Toxoplasma-*free subjects*

Personality profiles of 224 men and 170 women, mostly university professors and students, were estimated by Cattell's personality questionnaire. After collecting the personality factors data, the subjects were tested for cellular immunity against *T. gondii* by IDHT. Sixty-three men (27·1 %) and 40 women (23·5 %) tested positive. The personality profiles (16 personality factors) of *Toxoplasma*-infected and *Toxoplasma*-free persons (Table 1) were compared with the MANCOVA test using gender and the result of IDHT as independent variables and the age as a covariate. The effect of the toxoplasmosis was not significant (Rao's R (16, 374) = 0·811, P = 0·67). However, toxoplasmosis-gender interaction was highly significant (Rao's R (16, 374) = 2·05, P = 0·0097). Of the 16 personality factors estimated by Cattell's questionnaire the 5 factors that apparently caused the difference (these with the highest specific effects), A (F(1, 389) = 11·3, P = 0·0008), G(F(1, 389) = 7·31, P = 0·003), L (F(1, 389) = 7·87, P = 0·005), N (F(1, 387) = 5·16, P = 0·024), and $Q3$

Table 1. List of 16 personality factors monitored by Cattell's questionnaire

(The names and characteristics in the left column are for persons with low values of the factor, those in the right column for persons with high values of the factor. Asterisks designate the factors responsible for differences between the sets of *Toxoplasma*-infected and *Toxoplasma*-free subjects (MANCOVA results). The labels ♂ and ♀ designate the trait which was positively influenced by *T. gondii* in the men's and women's subset, respectively (discriminant function analysis).)

Sizothymia Reserved, detached, critical	*A**	Affectothymia ♀ Warmhearted, outgoing, easygoing
Low intelligence	*B*	High intelligence
Ego weakness	*C*	High ego strength
Submissiveness	*E*	Dominance or ascendance
Desurgency Sober, taciturn, serious	*F*	Surgence Enthusiastic heedless, happy-go-lucky
Low superego strength ♂ Disregards rules, expedient	*G**	Superego strength or character Conscientious, persistent, moralistic, staid
Threctia	*H*	Parmia
Harria	*I*	Premsia
Alaxia ♀ Trusting, accepting conditions, tolerant	*L**	Protension ♂ Suspecting, jealous, dogmatic
Praxernia	*M*	Autia
Naiveté Forthright, unpretentious	*N**	Shrewdness Astute, worldly, polished
Untroubled adequacy ♀ Self-assured, placed, secured	*O*	Guilt proneness ♂ Apprehensive, self-reproaching, insecure
Conservatism of temperament	*Q1*	Radicalism
Group dependency ♂ Sociably group dependent, "joiner"	*Q2*	Self-sufficiency ♀ Self-sufficient, resourceful, prefers own decisions
Low self-sentiment integration Uncontrolled, lax, follows own urges	*Q3**	High strength of self sentiment Controlled, exacting will power, socially precise
Low ergic tension	*Q4*	High ergic tension

($F(1, 387) = 5{\cdot}39$, $P = 0{\cdot}021$) are indicated and described in Table 1. Because an opposite-directions-shift of these factors was observed in men and women, we decided to analyse these two subsets separately.

To reveal which personality factors differ because of their association with toxoplasmosis and which ones differed because of their correlation with other (toxoplasmosis associated) personality factors we employed a logistic regression and a discriminant function analysis. Because both methods gave very similar results, we present only the results of the discriminant function analysis. This statistical method was primarily designed for classification of objects into previously defined groups. It can also be used for an elimination of correlation effects between factors by an approach based on analysis of covariance (Bouska *et al.* 1990). We classified either men or women into *Toxoplasma*-infected and *Toxoplasma*-free groups by their personality profiles. In the men's subset the factors *L*, *G*, *O*, and *Q2* entered classification function. In the group of 18 men classified by their personality profiles the frequency of IDHT positive persons was 72·2% (*a priori* frequency for our sample was 27·1%). In the women's subset the factors *A*, *L*, *O*, and *Q2* entered classification function and among 19 women classified as *Toxoplasma*-infected the frequency of IDHT positive persons was 63·2% (*a priori* frequency was 23·5%).

The personality profile-based 'diagnosis' of toxoplasmosis performed ineffectively within the negative subset. Among 206 men and 151 women classified as *Toxoplasma*-free the frequency of correct diagnosis was only 75·7% (*a priori* frequency 72·9%) and 81·5% (*a priori* frequency 76·5%), respectively. This may suggest that while the development of anti-toxoplasma immunity takes a short time, the transformation of human personality (and the manifestation of the changes) could be a prolonged process.

Correlation between the extent of personality shifts and the duration of toxoplasmosis

The possible existence of time-lag between the infection and the personality changes offers the possibility of deciding the causation of the phenomenon, namely to test if toxoplasmosis induces the personality factor-shift or if the combination of personality factors influences the probability of being infected by *T. gondii*. To answer this question we distributed the Cattell's questionnaire to 550 men in which the acute toxoplasmosis was diagnosed during the past 13 years. We received data for 190 patients for whom the clinical records were available (including IgM and IgG titres) and therefore the duration of latent toxoplasmosis was known. Fifteen men infected within the past 6 months and 11 men diagnosed for toxoplasmosis before the age of 6 were

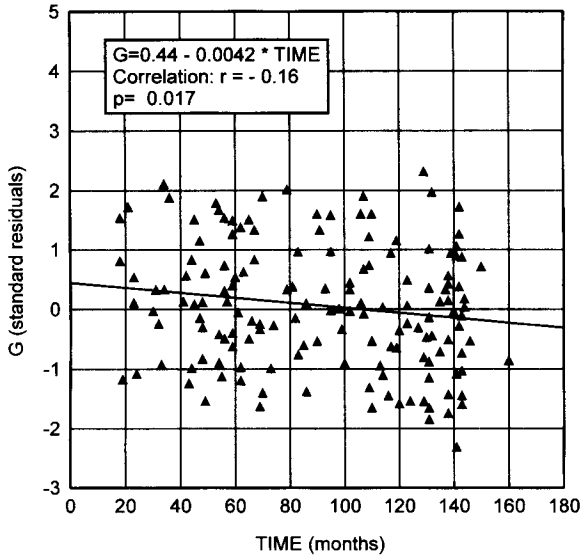

Fig. 1. Correlation between the length of infection and superego strength. The abscissa shows the residuals of regressions between age and the raw personality factor *G*, the ordinate shows the time (in months) from the first positive test for acute toxoplasmosis.

excluded from the analysis (see the Discussion section). The influence of the duration of toxoplasmosis on the age-non-standardized personality factors was estimated with regression analysis using the age of a person as a covariate. From 16 factors studied, only *G* (superego strength) systematically changed (decreased) during the 13 years following *T. gondii* infection ($R^2 = 0{\cdot}02$, $t(162) = 2{\cdot}14$, $P = 0{\cdot}017$, one-tailed *t*-test) (see Fig. 1). It was the same factor that was significantly lower ($F(1, 221) = 5{\cdot}92$, $P = 0{\cdot}016$) in *Toxoplasma*-infected men in our first experimental set (Biologists). A statistically insignificant tendency also existed ($R^2 = 0{\cdot}016$, $t(162) = -1{\cdot}88$, $P = 0{\cdot}062$, a two-tailed *t*-test) for the decrease of *B* (intelligence). This decrease became significant ($P = 0{\cdot}014$) when the data of 11 persons diagnosed with toxoplasmosis before the age of 6 (possibly congenital toxoplasmosis) were also included in the analysis.

DISCUSSION

Our results demonstrate the existence of a correlation between anti-toxoplasma immunity (monitored by IDHT) and certain personality factors in men and women. The existence of a correlation between the extent of personality factor shift and the duration of toxoplasmosis suggests that toxoplasmosis induces a shift in human personality, rather than the personality factor shift influences the probability of being infected with *T. gondii*.

The results from the MANCOVA suggest that personality factors *G*, *L*, *O*, *A*, and *Q3* might be shifted in *Toxoplasma*-infected men, and factors *A*, *L*, *N* and *Q3* in *Toxoplasma*-infected women (results not shown). On the other hand, in the discriminant function analysis another group of factors (*L*, *G*, *O*, *Q2* for men and *A*, *L*, *O*, *Q2* for women) proved to be most useful for the identification of *Toxoplasma*-infected subjects. This discrepancy can be explained by differences in the mathematical background of these two methods. Discriminant function analysis includes a stepwise covariance analysis. In every step, *F*-to-enter values are affected by the variables already present in the classification function. When a strong correlation exists between two variables (e.g. factor *G* and *Q3*) only the one with a higher *F*-value might enter the classification function. On the other hand, when low or no correlation exists among variables, all might enter the function despite their relatively low *F* values in the step zero of discriminant function analysis (or in MANCOVA).

The nature of the influenced factors (see Table 1) as well as the fact, that the same factors are often shifted in the opposite direction in the men and women subsets, make the biological or psychological interpretation of the toxoplasmosis-induced changes of the personality profiles very difficult. It has been demonstrated that *T. gondii*-infected animals (rodents) are less anxious (Hutchison *et al.* 1980*a*), less neophobic (Webster *et al.* 1994), more active (Hutchison, 1980*a*; Webster *et al.* 1994) and aggressive (Arnott *et al.* 1990) than the controls. It can be speculated whether the low superego strength, i.e. tendencies to disregard the societal rules, may be determined or influenced by lack of fear of punishment and/or by an aggression in men and by another factor in the women. Analogically *A* (affectothymia), i.e. warmheartedness, outgoingness, easygoingness may be controlled or influenced by lack of fear in the women, and by other factor(s) in men, depending on the difference between men's and women's social roles. The existence of gender-specific differences in the composition of certain personality factors is suggested by the difference in the structures of covariance matrices of Cattell's personality factors for men and women (results not shown).

It must be also stressed that the character of toxoplasmosis induced changes in the behaviour of humans and rodents may be dramatically different even if they are induced by the same mechanism. In the rodent system the ability to decrease neophobia and anxiety and to increase the activity of its intermediate host is highly adaptive for *Toxoplasma*. Such manipulation can positively influence the probability of transmission of *T. gondii* into the definitive host (felid) by carnivorism. In modern man such parasite activity is non-productive so the parasite is expected to be better adapted for manipulation of rodent behaviour. The changes in human behaviour (monitored by the changes in the personality profiles in our study) probably only indirectly reflect some activity of *T. gondii*, possibly the synthesis or induction of synthesis of dopamine

(Stibbs, 1985) or of other biologically active substances (Silverman & Varela, 1958) in the host brain tissue.

In our previous study (Flegr & Hrdy, 1994) we found effects of latent toxoplasmosis on the personality profile of men (not women). This is also the reason we chose male toxoplasmosis patients for our study of correlation of the extent of personality factor-shift with the duration of *T. gondii* infection. The present reanalysis of the old and new data showed that after the application of the finer method of the elimination of the effect of age, the results of statistical tests were different than originally reported. The difference between *Toxoplasma*-infected and *Toxoplasma*-free women became significant and the significance of the shift of factor *G* increased and of the factor *L* decreased for men. Our original inability to recognize the increase of the factor *A* in women was caused partly by lower *n* (143) and partly by the information loss caused by use of age-standardized personality factors, instead of the age-non-standardized data with age as a covariate. The main reason why the former approach should be avoided is that in the general population for which the age correcting-factors are tabulated and published the frequency of *Toxoplasma*-infected subjects and especially the kinetics of an age-dependent increase of this frequency (Robertson, 1966) can be different from that of an experimental set.

The data from 15 patients infected within the past 6 months were excluded from our correlation analysis. Acute toxoplasmosis often shows a symptomatic period with fever, general malaise, headache, dizziness, sore throat, coughing. Accompanying psychopathological features are very common and frequently include depression, apathy and anxiety, recurring anxiety spells, and paraesthesia (Ladee, Scholten & Posthumus Meyes, 1966). Many of these symptoms may be toxoplasmosis-non-specific. In our study a dramatic shift in personality profiles was detected in a group of 15 patients recently infected by *T. gondii* as well as in a group of 43 patients with toxoplasmosis-like symptoms but with negative results in toxoplasmosis immunological tests (complement-fixing reaction, ELISA IgM, ELISA IgA, indirect fluorescent antibody test) (data not shown). Similar effects of acute toxoplasmosis have already been reported by others (Höschl & Balon, 1980).

The data from 11 men diagnosed with toxoplasmosis before age 6 and therefore suspected of having a congenital form of toxoplasmosis were also excluded from the analysis. The neurological manifestation of congenital toxoplasmosis due to meningoencephalitis is relatively frequent, and the sequelae includes psychomotor and mental retardation (Koppe & Rothova, 1989). We suppose that the observed correlation between the decrease of factor *B* (intelligence) and the length of latent toxoplasmosis might be caused by the presence of unrecognized cases of congenital toxoplasmosis in our acquired toxoplasmosis experimental set (mainly within the long-duration toxoplasmosis subset).

The influence of severe forms of acute toxoplasmosis on human personality has been reported by many clinicians (Burkinshaw, Kirman & Sorsby, 1953; Minto & Roberts, 1959; Ladee *et al.* 1966; Freytag & Haas, 1979). In the literature, attention is frequently focused on psychoses with schizophrenic features that accompany latent toxoplasmosis or toxoplasmosis acquired in childhood or early adult life (for review see Ladee *et al.* 1966). Numerous studies have also shown an excess of *Toxoplasma*-infected subjects among patients in mental hospitals (Robertson, 1966; Thalhammer, 1962; Garcia, 1979; Garrido *et al.* 1978). Typically, however, the effects of acquired toxoplasmosis on immunocompetent subjects are mild; only a negligible fraction of infected subjects ever learn that they are parasitized. Latent toxoplasmosis acquired in adult life is usually considered asymptomatic (Remington, 1974). In this respect the existence of easily detected differences between *Toxoplasma*-infected and *Toxoplasma*-free biologists was unexpected. One can only speculate, whether these activities of the parasite are connected with an attempt (in modern humans a non-productive one) of the parasite to manipulate the host behaviour, or are only byproducts of a non-specific decline in the quality of host life. Infected subjects might theoretically suffer more frequent or more severe diseases because of an interference by the parasite with their immune system (Krahenbuhl & Remington, 1982; Remington & Krahenbuhl, 1982). Such effects of toxoplasmosis, however, have never been reported.

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