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Correlation of duration of latent *Toxoplasma gondii* infection with personality changes in women

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Abstract

Many parasites induce characteristic changes in behavior of their hosts. In humans latent toxoplasmosis is associated with changes in personality profiles. It has been already shown that a decrease in superego strength is correlated with duration of toxoplasmosis in men. Here we studied changes in personality profiles with Cattell's 16 PF questionnaire in *Toxoplasma*-infected women. The changes were measured as differences in personality factors between *Toxoplasma*-infected subjects and uninfected controls of the same age. The low-rate changes were studied in 230 women diagnosed with acute toxoplasmosis during past 14 years. The results showed the correlation between duration of toxoplasmosis and level of factors G (high superego strength) and Q3 (high strength of self sentiment). The high-rate changes were estimated by measuring the correlation between level of *Toxoplasma*-antibody titers (which rapidly decline after the end of acute phase of toxoplasmosis) and personality factors in an experimental set of 55 young mothers with latent toxoplasmosis. Again, certain factors, namely A (affectothymia), F (surge), G (high superego strength), H (parmia), and L (protension), correlated with the length of the infection. We suggest that the parasite induced the changes in the personality profiles of the women because of our observation of an increasingly different personality profile over time between women with latent infection and controls. The same evidence questions the view that women with a particular personality

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profile are more prone to acquisition of *T. gondii* infection. © 2000 Elsevier Science B.V. All rights reserved.

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1. Introduction

A growing list of parasitic species are known to influence the behavior of their host to increase the probability of their transmission to a new host (Barnard & Behnke, 1990; Poulin, 1994, 1995). The parasites often modify the behavior of their intermediate host to increase its susceptibility to predation and therefore the probability of their transmission to a definitive host. One popular model for studying the manipulation activity of parasites is the *Toxoplasma gondii* — rodent system. *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), cysts are formed mainly in neural and muscular tissues. The parasites (bradyzoites) inside the cysts usually cause little harm to an immunocompetent host and probably persist as viable parasites for the lifetime of the host (Remington & Krahenbuhl, 1982). The transmission of bradyzoites to a definitive host, a cat, occurs when the cat eats an infected host. Observed changes in the behavior of infected rodents; such as decrease of anxiety (Hutchison et al., 1980b) and neophobia (Webster et al., 1994; Berdoy et al., 1995), increase in activity (Hutchison et al., 1980a; Webster, 1994) and aggressiveness (Arnott et al., 1990), can be easily interpreted as the parasite adaptations that increase risk of predation. The physiological mechanism involved is unknown. However, indirect evidence suggest that the parasite influences the synthesis of some neurotransmitter, possibly dopamine (Varela et al., 1956, 1957; Stibbs, 1985). In aberrant (non-rodent) host the behavioral changes induced by changes in the neurotransmitter level would be probably nonadaptive from the point of view of *T. gondii* survival (they have never been a subject of natural selection). However, any changes in the neurotransmitter levels could induce changes in personality profile of the subject (Cloninger, 1987; Asberg, 1997; Curtin et al. 1997). The high prevalence of latent *T. gondii* infections in different countries (about 20% of pregnant women in Finland (Lappalainen et al., 1992), 27% in Denmark (Lebech et al., 1993), 40% in southern Italy (Buffolano et al., 1996), and 84% in Paris (Desmonts & Couvreur, 1974)) offers the opportunity to assess the changes by using personality questionnaires. It has already been reported (Flegr & Hrdý, 1994; Flegr et al., 1996) that *Toxoplasma* positive and *Toxoplasma* negative students differ in the personality factors A (affectothymia), G (superego strength), L (protension), N (naiveté) and Q3 (strength of self sentiment), (all factors were measured with Cattell 16 PF questionnaire, form A). It has also been shown that a correlation ($r = -0.16$, $P = 0.017$) exists between the length of *T. gondii* infection and the factor G (superego strength) in a group of men diagnosed with acute toxoplasmosis in the past 13 years (Flegr et al. 1996). Authors suggested that the existence of such correlation supported the hypothesis that toxoplasmosis induced a shift in human personality and made less probable the opposite hypothesis (i.e. that the personality factor shift influenced

the probability of acquiring a *T. gondii* infection). For women, a similar study on causal relationships between personality changes and latent toxoplasmosis is missing.

The aim of the present study was to search for positive correlation between the length of latent *T. gondii* infection and amount of personality factor shift (measured as differences in personality factors between *Toxoplasma*-infected subjects and uninfected controls of the same age) in two different sets of women (230 acute toxoplasmosis patients and 55 young mothers diagnosed with latent toxoplasmosis during pregnancy). The existence of such positive correlation would suggest that manipulation or pathogenic activity of the parasite probably induces the differences in personality profiles observed in *Toxoplasma*-infected subjects. On the other hand, absence of such positive correlation or an existence of negative correlation would suggest that the subjects with particular personality profiles have higher chances to be infected by *T. gondii*.

2. Experiment I: correlation between personality factor shifts and duration of latent toxoplasmosis in acute toxoplasmosis patients

2.1. Methods

2.1.1. Subjects

The experimental set ‘acute toxoplasmosis patients’ was composed of 230 women diagnosed with acute toxoplasmosis within a 14 year period in various hospitals in central Prague. Five hundred and ten subjects were mailed the personality questionnaire 27–178 months after the first positive serological test for the toxoplasmosis. They were informed that the research project in which they could voluntarily participate concerned the correlation between the human personality profile and probability of *T. gondii* infection. We obtained personality data from 230 women (45%).

The method of experimental subject recruitment as well as the personality data handling respected all rules of current Czech legislation.

2.1.2. Personality tests

Cattell’s sixteen factor questionnaire (form A) (Cattell, 1970) was used for characterization of personality profiles. This questionnaire is still widely used for personality studies in many countries, including the Czech Republic (Christiansen et al., 1994; Grossman & Craig, 1995). It covers sixteen personality factors (Table 1). The main advantages of this traditional questionnaire are that it can be completed by most subjects within 40 min and that the data can be directly compared with results of our previous parasitological studies (Flegr & Hrdý, 1994; Flegr et al., 1996, 1998; Flegr & Havlíček, 1999).

2.1.3. Immunological tests for toxoplasmosis

The serological and clinical data were obtained from our database of patients at the Prague Public Health Center. Acute toxoplasmosis was diagnosed on the basis

of clinical symptoms (lymphadenopathy, rash, fever, lymphocytosis, tonsillitis or bronchopneumonia) and results of several 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).

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

Sizothymia Reserved, detached, critical	A	Affectothymia Warm-hearted, outgoing, easygoing
Low intelligence	B	High intelligence
Ego weakness Affected by feelings, emotionally less stable	C	High ego strength Stable, mature, faces reality, calm
Submissiveness Obedient, mild, easily led, docile	E	Dominance or ascendance Aggressive, competitive, stubborn
Desurgency Sober, taciturn, serious	F	Surgency Enthusiastic, heedless, happy-go-lucky
Low superego strength Disregards rules, expedient	G	Superego strength, character Conscientious, persistent, moralistic, staid
Threctia Shy, timid, restrained	H	Parmia Adventurous, 'thick-skinned', socially bold
Harria Tough-minded, rejects illusions	I	Premsia Tender-minded, sensitive
Alaxia Trusting, accepting conditions, tolerant	L	Protension Suspecting, jealous, dogmatic
Praxernia Practical, has 'down-to-earth' concerns	M	Autia Imaginative, bohemian
Naivieté Forthright, unpretentious	N	Shrewdness Astute, worldly, polished
Untroubled adequacy Self-assured, placed, secured	O	Guilt proneness Apprehensive, self-reproaching, insecure
Conservatism of temperament Conservative, respecting	Q1	Radicalism Experimenting, liberal, analytical
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 Relaxed, tranquil, torpid	Q4	High ergic tension Tense, frustrated, driven, overwrought

^a 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.

2.1.4. Statistics

The Statistica® 5.1 program was used for all statistical testing: A multiple linear regression was used to estimate the correlation between the length of latent toxoplasmosis and the extent of personality factor-shift in acute toxoplasmosis patients.

The raw data (age-nonstandardized) from the questionnaire were used in all statistical analyses to prevent information loss during the transformation of twenty seven-point raw scales into ten-point age-standardized scales and to avoid an application of general population-based correction factors on the potentially 'non-standard' subpopulations of toxoplasmosis patients.

2.2. Results

The multiple regression analysis of personality data from 230 women with latent toxoplasmosis showed that among the five factors (A, G, L, N, Q3) which are expected to be influenced by toxoplasmosis on the basis of results of previous studies, only G (superego strength) and Q3 (strength of self sentiment) systematically changed (increased) during the 14 years following the *T. gondii* infection (see Fig. 1 and Table 2a and b). Statistical significance (*P*) of the changes in one-sided tests (the increase was a priori expected on the basis of earlier studies) was < 0.01 ($R^2 = 0.02$, $t(225) = 2.35$) and < 0.015 ($R^2 = 0.02$, $t(126) = 2.21$) for the personality factors G and Q3, respectively. After the most conservative Bonferroni's correction for multiple tests the significance level for the G and Q3 was 0.049 and 0.071, respectively.

3. Experiment II: correlation between duration of latent toxoplasmosis and personality factors in young mothers

3.1. Methods

3.1.1. Subjects

The experimental set 'young mothers' consisted of 55 women 18–39 years old who were serologically tested for toxoplasmosis during pregnancy. Eight hundred and thirty pregnant women tested for anti-*Toxoplasma* antibodies were sent a Cattell's questionnaire. We obtained personality data from 191 mothers (23%) (136 anti-*Toxoplasma* antibodies negative and 55 anti-*Toxoplasma* antibodies positive). Comparison between *Toxoplasma*-negative and *Toxoplasma*-positive women was not a subject of present study and was published elsewhere (Flegr & Havlíček, 1999). *Toxoplasma*-positive women had *Toxoplasma*-antibody titres between 1:8 and 1:64, indicative of latent toxoplasmosis. Based on the levels of IgG and IgM antibodies measured in ELISA tests no woman involved suffered acute toxoplasmosis. All subjects received the personality questionnaire 6–7 months after the serological examination, mostly 2–5 months after the childbirth. In the cover letter they were only asked to voluntarily participate in an unspecified research project. According to our experience, a relatively low response rate in the young mothers set (23%) was probably caused by the fact that only very general information about the aim of the

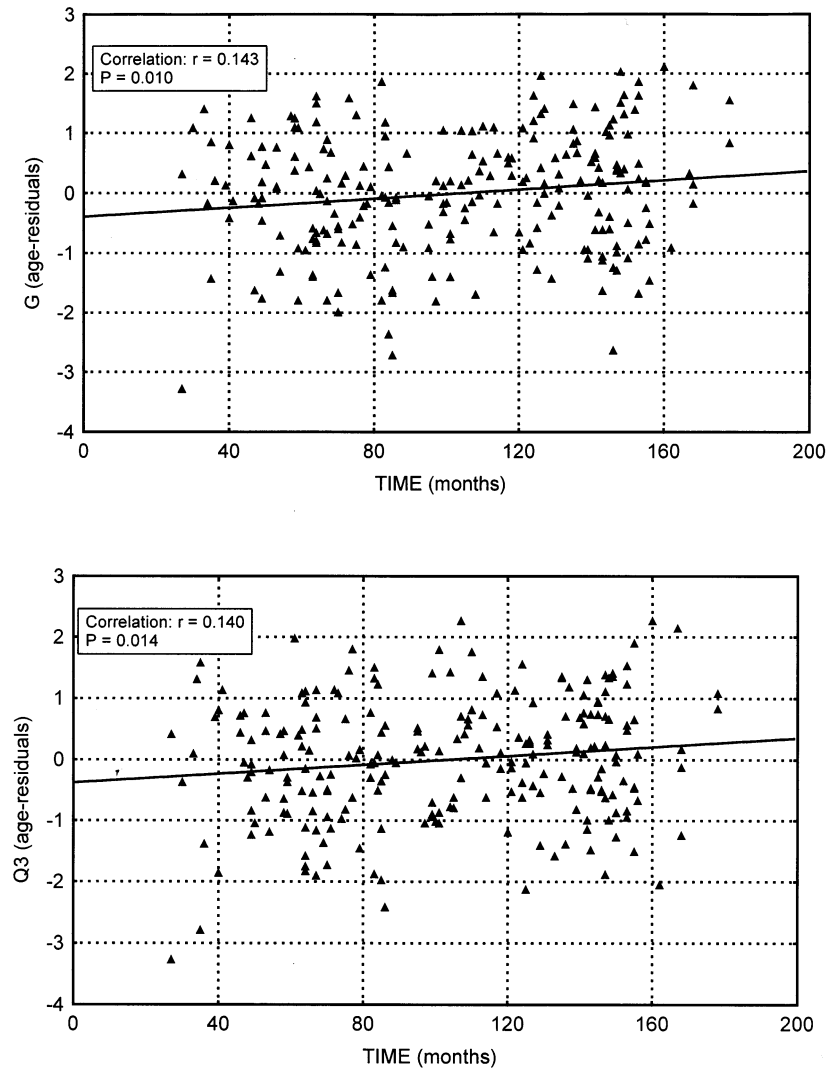


Fig. 1. Correlation between the length of infection and personality factors shifts. The abscissa shows the residuals of multiple regression between age and the raw personality factor (section 2.1), the ordinate shows the time (in months) from the first positive test for acute toxoplasmosis. The statistical significances are shown for one-sided tests because of an existence of a priori knowledge about the direction of shifts.

project was provided in the cover letter. We intentionally did not mention *T. gondii* in the letter to avoid a possible fear of young mothers of congenital toxoplasmosis.

3.1.2. Personality test

Cattell's 16 factor questionnaire (form A) (Cattell, 1970) was used for characterization of personality profiles.

3.1.3. Immunological tests for toxoplasmosis

The serological and clinical data were obtained from our database of patients at the National Diagnostic Laboratory for Toxoplasmosis, National Institute of Public Health, Prague, Czech Republic. The latent toxoplasmosis in pregnant women was diagnosed with CFT (Warren & Sabin, 1942). The CFT titre of anti-*Toxoplasma* antibodies in sera was measured in dilutions between 1:8 and 1:1024. All subjects with the titres from 1:8 to 1:64 were considered latent toxoplasmosis positive (and were retested for possible acute toxoplasmosis with ELISA tests), the subject with titres lower than 1:8 were negative. No subjects with titres equal or higher than 1:128 or with other indication of recent acute toxoplasmosis (e.g. high titres in IgG and IgM ELISA) were involved into our study.

3.1.4. Statistics

For testing of correlation between the anti-*Toxoplasma* antibodies titres (four-points ordinal scale 1, 2, 3, 4 for titres 1:8, 1:16, 1:32, and 1:64, respectively) and the extent of personality factor shift we used nonparametric Kendall tests (Statistica[®] 5.1). The effect of age was controlled by using residuals of multiple regression between two variables, i.e. age and second power of age (independent variables) and raw personality factors (dependent variable) instead of raw personality factors in our Kendall test. It was found that if a second-order polynomial replaced the first-order polynomial in usual age-standardization procedure (Flegr et al., 1996) it would lower the residual errors.

3.2. Results

The actual duration of latent toxoplasmosis in young mothers is unknown because acquired toxoplasmosis is usually asymptomatic and most of the infected people never learn that they are parasitized by *T. gondii*. However, the probable duration of toxoplasmosis can be estimated from the level of anti-*Toxoplasma* antibodies which is very high in early infections and decreases during months and first years after the end of acute toxoplasmosis. The correlation between the level of antibody titers and personality factors of 55 *Toxoplasma* positive young mothers was estimated by Kendall nonparametric regression. Table 2b shows that several factors, including *A* (Tau = -0.255, $P = 0.003$) and *G*, (Tau = -0.206), $P = 0.013$) (Fig. 2) significantly correlate with the antibody level (and therefore with the duration of toxoplasmosis). Correlation for the factor *A* was highly significant ($P = 0.015$) even after the Bonferroni's correction for multiple tests. The negative correlation between the personality factors and antibody level reflects in fact the existence of positive correlation between the personality factors and length of the infection. Therefore, the results of experiment 2 were in perfect agreement with those of experiment 1 and with the results published elsewhere (Flegr et al., 1996; Flegr & Havlíček, 1999).

4. General discussion

Existence of correlation between length of latent toxoplasmosis and certain

Table 2
Correlation between Cattell's personality factors and length of latent toxoplasmosis^a

Factor	230 women diagnosed with acute toxoplasmosis within the past 14 years						
	Mean	S.D.	Mean old	Mean fresh	<i>r</i>	<i>P</i>	<i>P</i> ^B
A	12.43	3.26	12.10	12.43	-0.023	0.726	NS
B	8.08	2.13	8.17	7.91	0.059	0.371	NS
C	13.13	4.03	12.93	12.83	-0.019	0.772	NS
E	12.13	4.24	11.94	11.89	0.005	0.941	NS
F	12.60	5.35	12.23	12.97	0.002	0.971	NS
G	11.85	3.96	12.69	11.10	0.143	0.010	0.049
H	12.12	6.25	11.93	11.66	0.032	0.631	NS
I	13.21	3.34	13.00	13.66	-0.036	0.587	NS
L	10.65	3.35	10.39	11.10	-0.020	0.770	NS
M	10.89	3.41	10.80	10.89	-0.055	0.413	NS
N	10.67	3.09	10.86	10.21	0.056	0.402	NS
O	11.26	4.21	11.44	11.64	0.040	0.546	NS
Q1	6.30	2.82	6.04	6.30	-0.011	0.872	NS
Q2	11.84	3.60	11.86	11.67	0.006	0.926	NS
Q3	11.70	3.25	12.25	10.77	0.140	0.014	0.071
Q4	14.04	4.39	14.07	14.53	0.003	0.961	NS
Factor	55 mothers diagnosed with latent toxoplasmosis during pregnancy						
	Mean	S.D.	Mean old	Mean fresh	Tau	<i>P</i>	<i>P</i> ^B
A	12.80	3.14	14.13	11.27	-0.255	0.003	0.015
B	8.93	1.85	9.00	9.2	0.091	0.328	NS
C	13.56	3.77	14.47	12.27	-0.171	0.065	NS
E	12.11	4.61	13.67	11.53	-0.097	0.295	NS
F	12.87	4.92	15.73	11.80	-0.269	0.004	NS
G	12.00	2.92	12.80	11.33	-0.206	0.013	0.065
H	12.67	5.90	15.40	10.53	-0.250	0.007	NS
I	12.35	3.18	12.80	11.87	-0.074	0.418	NS
L	10.44	3.55	10.93	9.00	-0.208	0.025	NS
M	11.05	3.02	11.53	10.47	-0.075	0.417	NS
N	10.29	3.20	9.87	10.20	0.069	0.460	NS
O	11.73	3.38	12.20	11.67	-0.079	0.393	NS
Q1	6.25	2.60	6.07	5.73	-0.058	0.532	NS
Q2	11.24	3.05	11.27	11.48	0.060	0.520	NS
Q3	11.55	3.29	11.67	12.27	0.033	0.725	NS
Q4	14.84	3.93	15.27	14.40	-0.017	0.853	NS

^a Patients: The second, third, fourth and fifth columns list the arithmetic mean of all 230 women, S.D., arithmetic mean for 70 women with oldest infections, and arithmetic means for 70 women with freshest infections, respectively. The sixth, seventh and eighth columns list the partial correlation coefficients, statistic significances and statistical significances after Bonferroni's correction, respectively of a multiple regression between personality factors and the duration of latent toxoplasmosis. (b) Young women: The second, third, fourth and fifth columns list the arithmetic mean of all 55 women, standard deviation, arithmetic mean for 15 women with lowest titres of antibodies (oldest infections), and arithmetic means for 15 women with highest titres (with freshest infections), respectively. The sixth, seventh and eighth columns list Kendall Tau coefficients, statistic significances and statistical significances after Bonferroni's correction, respectively of a nonparametric regression between age-standardised factors and the anti-

personality factors, namely A (affectothymia—i.e., warmheartedness, outgoingness, easygoingness), G (superego strength – i.e., conscientiousness, persistence), and Q3 (strength of self sentiment — i.e. high will power, social preciseness) was found in two experimental sets of women, the acute toxoplasmosis patients, and the young mothers. The same factors were reported to be associated with latent toxoplasmosis in previous study in an independent experimental set (female students of biology). The correlation between the extent of personality factor shift (estimated by comparison of personality profiles of *Toxoplasma*-infected subjects and controls) and the duration of toxoplasmosis seems to suggest that the toxoplasmosis induces the shift in human personality, rather than the personality factor shift influences the probability of being infected with *T. gondii*.

Positive correlation between the factor A and toxoplasmosis was observed in students (Flegr et al., 1996) and young mothers (present study) but not in the acute toxoplasmosis patients. This discrepancy could be explained by the fact that acute patients were observed during the period from 27 months to 14 years after first diagnosis of toxoplasmosis. If the change of the factor A is very rapid, it could be assessed by comparison of *Toxoplasma* negative and positive subjects (Flegr et al., 1996; Flegr & Havlíček, 1999) or by testing the correlation between the extent of the change of the factor and decrease of antibody titers (which occurs within months or few years after the end of acute toxoplasmosis). However, the change could be already completed in acute patients at the beginning of our observation period, i.e., more than two years after the diagnosis of acute toxoplasmosis. Analogical explanation (this time a slow rate of the change) can be found for the fact that correlation between length of toxoplasmosis and the factor Q3 was not observed in the young mothers set. It must be also stressed that despite relatively high statistical significance of correlation tests the total amount of variability of personality factors that can be explained by the length of latent toxoplasmosis is rather low. Therefore, large data sets must be analyzed to detect the effect of latent toxoplasmosis.

It is difficult to reveal which personality factors were directly influenced by toxoplasmosis and which were influenced only indirectly because of their correlation with other (toxoplasmosis influenced) factors. Our previous results suggest that the factors G and Q3 are strongly correlated even in the *Toxoplasma* negative subjects (Flegr et al., 1996). Also factor A is strongly correlated with several other personality factors (F, G, I, L, and Q2). It is indicative that after the elimination of effect of the factor A on remaining factors (by computing standard residuals of linear regression between age-residuals of factors B...Q4 and the age-residual of factor A) the significant correlations between antibody level and the shift of the factors H and L in the young mothers virtually disappear. Therefore, it is likely that only factors A, G and O are in fact directly influenced by the toxoplasmosis while other factors

Toxoplasma antibody titre (reflecting the duration of latent toxoplasmosis). (a) and (b) Because of an existence of *a priori* knowledge about the direction of the toxoplasmosis-associated shift in the factors A, G and Q3, the table lists the results of these factors in one-sided tests. For all other factors the results of two sided tests are shown. For five factors (A, G, L, N, Q3) that were known to be shifted in *Toxoplasma*-positive women the Bonferroni's correction was done by multiplying the *P* by 5, for all other factor by 16. NS means nonsignificant result after Bonferroni's correction, i.e. $P^B < 0.1$.

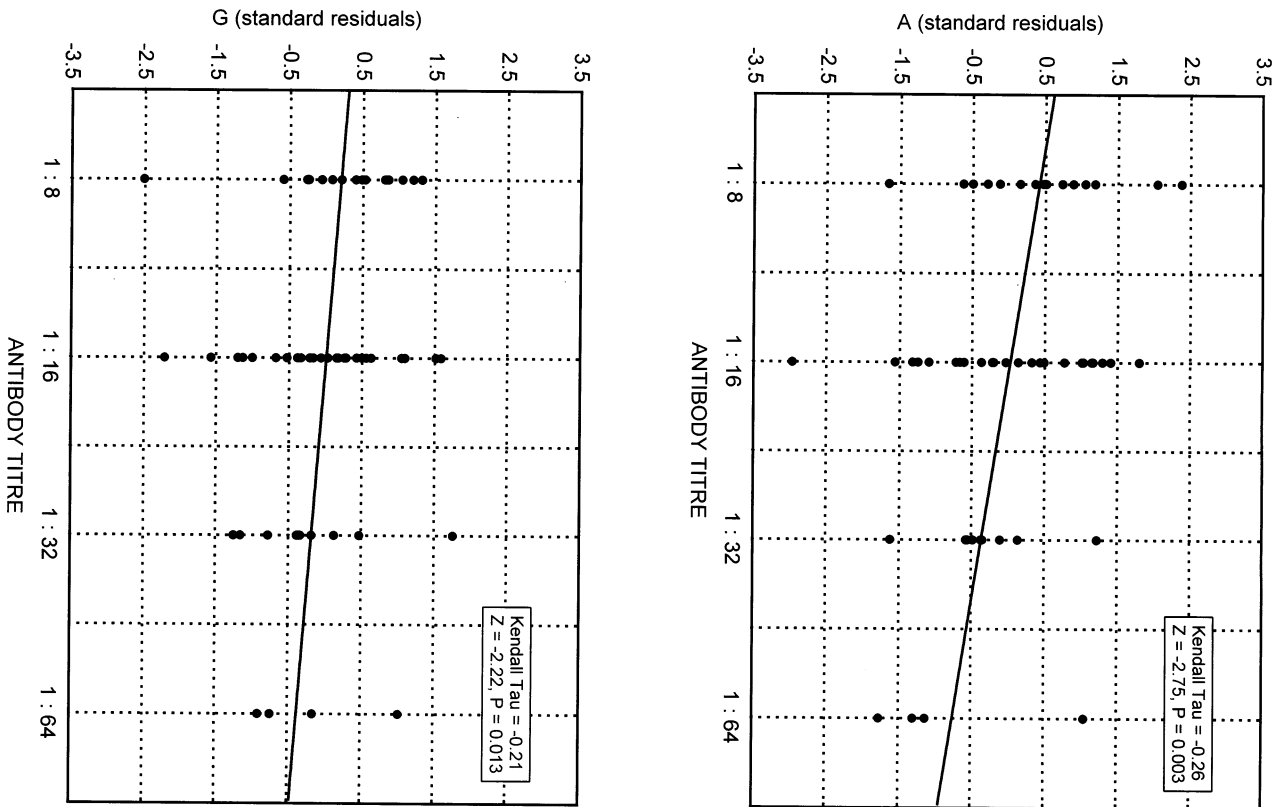


Fig. 2. Correlation between the anti-*Toxoplasma* antibody titre (reflecting the length of infection) and personality factors shifts. The abscissa shows the residuals of multiple linear regression between age and the raw personality factor (Section 2.1), the ordinate shows the antibody titre measured with CFT. The statistical significances are shown for one-sided tests because of an existence of a priori knowledge about the direction of shifts. (The negative correlation between the personality factors and antibody level reflects the positive correlation between the personality factors and length of the infection.)

are influenced only indirectly (because of their correlation with *Toxoplasma* influenced factors).

Important differences between women (this study and (Flegr & Havlíček, 1999)) and men (Flegr et al., 1996) were observed in the *T. gondii* induced personality profile changes. With the exception of the factor O, all factors shifts were always in opposite direction in men and women. It has been already reported for five factors (A, G, L, N, and Q3) (Flegr et al., 1996). In the present study we found a similar tendency for these opposite-direction shifts also for the factors C, H, Q1, Q2, and Q4. We can only speculate whether the effect of toxoplasmosis is really gender-specific or whether all subjects are in fact shifted in the same direction but either men or women try to conceal the real character of changes in their personality.

The nature of the influenced personality factors (see Table 1) as well as the fact that many factors are shifted in the opposite direction in men and women make the biological or psychological interpretation of toxoplasmosis-induced changes of the personality profiles very difficult. It has been demonstrated that *T. gondii*-infected rodents are less anxious (Hutchison et al., 1980b), less neophobic (Webster et al., 1994; Berdoy et al., 1995) and more active (Hutchison et al., 1980a; Webster, 1994) than the controls. It could be speculated that the nature of these changes recall the increase of factors A and Q2 identified with logistic regression (Flegr et al., 1996) in women. It must be stressed that because of evolutionary plasticity of neuroregulatory mechanisms, the character of toxoplasmosis induced changes in the behavior of humans and rodents may be dramatically different even if they are induced by the same process, e.g. by production or induction of production of the same neurotransmitter in the host brain tissue.

In this study the Cattell's 16PF questionnaire was used for monitoring personality profiles of infected subjects. The main reason for using this questionnaire was to make possible a direct comparison of results with those already published in four previous studies. At present several personality questionnaires are available which might be better suited for studies such as ours. For example, questionnaires are currently available which purport to assess personality factors correlated with activity in a specific monoaminergic pathway. We strongly support the replication of the current work using such questionnaires that are grounded in current psychobiological approaches.

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