Vigilance/Sustained Attention Abnormalities in Subjects with Latent Toxoplaxmosis

Odchylky vigilance/udržované pozornosti u osob s latentní toxoplazmózou

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SUMMARY

Healthy controls without any mental disorder participated in the project 'Psychosocial and biological predictors of therapeutic outcome of chronic affective and psychotic disorders'.

Methods: A total of 115 persons (65 women, 56.5%) completed the computerized test Conners' Continuous Performance Test II Version 5 for Windows (CPT II V.5), and were interviewed for depression, demographic and health status. All participants were serologically tested and reliably divided into *Toxoplasma* negative or positive subgroups.

Results: Toxoplasma positive subgroup of healthy subjects showed statistically significant tendency to improve their performance in the course of the test expressed by Hit Reaction Time Block Change parameter in Conner's CPT II.

Conclusion: We found out gradual improvement of attention/vigilance in healthy toxoplasma-infected subjects using specific method. The overall acceleration of reaction times may be related to attention deterioration of *Toxoplasma* cyst carriers at the beginning of the test and their preserved capacity to balance early vigilance decrement. This result represents a first step to examine long-term neurotropic effect of latent TG parasitosis on psychotic and non-psychotic population.

Key words: *Toxoplasma gondii*, attention, vigilance, gene and environment interaction, Conner's CPT II., infectious theory of schizophrenia

SOUHRN

Do projektu „Psychosociální a biologické prediktory efektu léčebných intervencí u chronických afektivních a psychotických poruch" se zapojili zdraví dobrovolníci s negativní psychiatrickou anamnézou.

Metodika: Celkem 115 osob (65 žen, 56,5 %) absolvovalo vyšetření počítačovým testem Conners' Continuous Performance Test II Version 5 for Windows (CPT II V.5) a vyplnilo dotazníky deprese, demografické a zdravotní údaje. Všichni účastnici byli sérologicky testováni a spolehlivě rozděleni na *Toxoplasma* séronegativní a séropozitivní podskupiny.

Výsledky: *Toxoplasma* pozitivní podskupina zdravých dobrovolníků vykazovala statisticky významnou tendenci zlepšovat svůj výkon v průběhu testu vyjádřenou pomocí parametru Hit Reaction Time Block v Conner's CPT II.

Závěr: Zjistili jsme pozvolné zlepšování pozornosti/vigilance u zdravých dobrovolníků infikovaných toxoplazmou za použití specifické metody. Celkové urychlení reakčních časů v průběhu testu se může vztahovat ke zhoršené pozornosti nositelů toxoplazmových cyst na počátku testu a jejich zachovalé schopnosti vyrovnat počáteční útlum pozornosti. Výsledky jsou prvním krokem při zkoumání dlouhodobého neurotropního efektu latentní toxoplazmové parazitózy na psychotickou a nepsychotickou populaci.

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Introduction

Toxoplasma gondii (TG) in the form of parasitic disease affects 20–80 % of people across the world depending on eating habits and exposure to cats (Tenter et al., 2000 in Flegr, 2007). It is currently supposed that probably all postnatally infected people bear dormant stages of TG, i.e. bradyzoites in zoitocysts (tissue cysts) located mainly in the neural and muscular tissue (Remington and Krahenbuhl, 1982). The tissue cysts, which are resistant to anti-parasitic drugs, remain infective until the end of the host life (Gross, 1996). Interestingly, the clinical consequences of long-standing, chronic infection have

been largely ignored (Holliman, 1997) and surprisingly few studies have been performed to seek associated disease and there is no research systematically examining the interaction of dormant toxoplasmatic cysts and human organism. Conventional opinion has been that latent *Toxoplasma* infection is usually asymptomatic and has no long-term sequelae unless the host becomes immune suppressed, when secondary reactivation of the infection can occur (Ho-yen, 1992). Results of animal studies and recent studies of personality profiles, behavior, and impaired psychomotor performance in healthy and schizophrenia subjects, however, have led to a reconsideration of this assumption (Flegr, 2007). Havlíček et al. (2001) demonstrated in a double blind study in healthy blood donors the increase of simple reaction times of subjects with latent toxoplasmosis. The prominent reduction in psychomotor performance occurred in the 2nd and 3rd minute of the test which indicates the role of deteriorated attention capacity in TG positive subjects. Similar results were recently obtained in several (unpublished) studies performed on Czech blood donors, biology students and military recruits (Flegr, 2007).

Another contribution to see behavioural differences between *Toxoplasma*-infected and *Toxoplasma*-free subjects are two traffic accident studies. The increased prevalence of antibodies to TG in individuals deemed to have been responsible for causing (either as a driver or as a pedestrian) a motor vehicle accidents suggested that the subjects with latent toxoplasmosis had a 2.65 times higher risk of traffic accidents than non-infected subjects in Prague (Flegr et al., 2002). Possible explanation of "poor traffic performance" in subjects with latent toxoplasmosis may be a consequence of impaired attention, working memory or the alteration in vigilance level. A higher incidence of TG antibodies among drivers involved in traffic accidents was also found in a recent study in Turkey (Yereli et al., 2006). Studies have also examined possible relationships between TG infection and intelligence, education, and memory. Initial reports of associations with intelligence and education (Flegr et al., 1996; Flegr et al., 2003) were found to be spurious when all confounding factors were taken into account (Novotná et al., 2008). Two unpublished studies found no association between infection and short-term memory (Flegr, 2007).

There are only inconclusive and sporadic findings of the effect of latent toxoplasmosis on cognitive performance in schizophrenia. Persons with schizophrenia who have serologic evidence of *Toxoplasma* infection have increased levels of cognitive impairment on Repeatable Battery for the Assessment of Neuropsychological Status (RBANS) compared to age-matched *Toxoplasma*-seronegative patients with similar degree of psychotic symptoms (Borronow et al., 2002). On the other hand Dickerson et al. (2007) did not find any difference in cognitive performance on RBANS between infected and non-infected schizophrenia sample, suggesting that cases associated with TG do not form distinct clinical or cognitive subgroup. Postal survey analysis carried out by Vavřinová (2005) revealed that there could be a psychomotor retardation in children of toxoplasma seropositive mothers.

Finally, there are 9 of 11 studies that show personality feature differences between TG-infected and uninfected group using Cattell's 16-personality factor (16PF) questionnaire (Flegr, Hrdý, 1994; Flegr et al., 1996; Flegr et al., 1998; Flegr, Havlíček, 1999; Flegr et al., 2000). The personality of infected men showed lower superego strength (rule consciousness) and higher vigilance (factors G and L on Cattell's 16PF). Thus, the men were more likely to disregard rules and were more expedient, suspicious, jealous, and dogmatic. The personality of infected women, by contrast, showed higher warmth and higher superego strength (factors A and G on Cattell's 16PF), suggesting that they were more warm hearted, outgoing, conscientious, persistent, and moralistic. Both men and women had significantly higher apprehension (factor O) compared with the uninfected controls. The subjects tested with Cloninger TCI (Temperament and Character Inventory) in 3 out of 5 studies showed a decrease in the novelty-seeking factor on the Cloninger TCI (Flegr, 2007). Decreased novelty seeking behaviour in *Toxoplasma*-infected subjects has been confirmed in three independent populations (male soldiers and male and female blood donors) (Skallová et al., 2006). Possible pathogenetic models for chronic Toxoplasma infection effect on brain and/or pathophysiology of schizophrenia were explained in detail previously (Flegr et al., 2003; Holub et al., 2006).

Study design

Cognitive impairment represents an essential area of interest in the project 'Psychosocial and biological predictors of therapeutic outcome of chronic affective and psychotic disorders'. The study design and assessment procedures have been comprehensively specified earlier (Holub et al, 2006). As induced alteration of cognitive functions is considered as an element of vulnerability for the development of some schizophrenia subtypes, it is reasonable to use standardized instrument to elucidate the possible involvement of latent toxoplasmosis in cognitive dysfunction. The continuous performance test (CPT) has a long history of use for measuring processes related to sustained attention/vigilance, reaction time, response inhibition, signal detection, impulsivity and other aspects of attentional processes (see reviews by Riccio et al, 2001; Conners, 2005). In this task, individuals are asked to press the space bar for all letters displayed on the computer screen except the letter X. There are six blocks, each displaying 60 letters at different interstimulus intervals. The test lasts approximately 14 minutes. CPT has not been adminstered yet in TG subjects and our study should for the first time verify previous simple reaction time deterioration using this highly sensitive instrument of sustained attention. Traditional measures include the number or percentage of errors of omission and errors of commission. Errors of omission occur when the participant fails to respond to the target stimulus. Errors of commission occur when the participant responds to a nontarget stimulus. In addition to these traditional measures, signal detection theory allows the incorporation of other measures of signal detectability (d'), response bias (ß), and reaction time (RT; Green and Swets, 1966). d' represents that portion of the signal-noise distribution attributable to veridical perception of the signal, whereas ß represents that portion of the distribution attributable to the subject's subjective threshold for making a response. If one makes the assumption that a faster reaction time (RT) represents the subject's easier discrimination of the target, then RT and variability in RT can serve as additional measures of detectability (Conners et al, 2003).

The goal of this sectional analysis was to examine whether there is a correlation between the serological evidence of latent toxoplasmosis in healthy controls and their computerized Continuous Performance Task II. (Conner's) performance.

Method

The control healthy population in our study was randomly chosen and matched with schizophrenia patients in the CNS Psychosocial and biological predictors of therapeutic outcome of chronic affective and psychotic disorders'project according to their gender, age and education. This project was reviewed and approved by the local ethical committee in Prague Psychiatric Center . The controls are representative of the same geographical area of Prague. Healthy volunteers included healthy members of staff working in Mental Hospital Bohnice, friends and family members of the staff and undergraduate medical students of the 3rd Medical Faculty of Charles University. Their physical and mental health status were determined through a health questionnaire. In the selection of both the schizophrenic and the healthy population, the presence of any immunological, auto-immune or long-term organ disorder, which could influence the immunological status, were considered as exclusion criteria. The subjects with a history of mental illness and alcohol or psychoactive substances abuse were also excluded from the control population. Patients and healthy controls were verbally and in writing explained the rational of the study, and they signed a consent form. The total number of healthy participants studied was 118, however, reassessment failed to unambigously differenciate the serological status of 3 participants that were excluded from the sample. Characteristics of study subjects are presented in Table 1. Toxopositive participants form an older sample comparing to toxonegative group. We found serological evidence of *Toxoplasma* infection in 24 (20.9 %) of the 115 controls. The individuals who had serological evidence of *Toxoplasma* did not differ from those who did not in terms of gender, race or educational level.

Measurements

All participants provided 2 ml of blood for serological testing. Specific anti-*Toxoplasma* IgG and IgM antibody concentrations were determined by ELISA (IgG: SEVAC, Prague, IgM: TestLine, Brno), optimized for early detection of acute toxoplasmosis, and the complement fixation test (CFT) (SEVAC, Prague), as the decrease of CFT titres is more regular and therefore better reflects length of *T. gondii* infections . Titres of antibodies to *Toxoplasma* in the sera were measured at dilutions between 1 : 8 and 1 : 1024. The subjects manifesting IgM negative by ELISA (positivity index < 0.9) and having CFT titres higher than 1 : 8 were considered latent-toxoplasmosis positive. All the measurements were performed by the same person in National Reference Laboratory for Toxoplasmosis within the National Institute of Public Health. Continuous Performance Task (CPT II. Conner's) computerized test and depression and medical history questionnaires were administred by the same trained person to avoid issues of inter-rater reliability. Administering person was blind to the hypothesis at the time of measurement and administration.

Statistical analysis

All data are presented as mean and standard deviation or rate of positive cases. According to the data distribution, differences were assessed using Student's t test or Mann-Whitney U test, respectively. Fisher exact test was used in case of qualitative variables. All tests were two-sided and an exact significance level of 0.05 was adopted. No Bonferroni correction was applied. Analyses were performed using Statistica 7.0 software.

Results

115 heathy volunteers (50 men and 65 women) were tested for specific immunity against *Toxoplasma*. The prevalence rates of Toxoplasma infection in men and women were 18,0% and 23,1%, respectively. Performance on the CPT for the *Toxoplasma*-free and *Toxoplasma*-infected groups are shown in Table 2. Overall, no significant differences in performance were found between infected and non-infected subjects. It is important to note that both groups performed well in regard to normative data and presented similar results in most CPT measures. Significant difference between groups was detected for CPT RT Block /t (113) = 2.70; p = 0.008/. Additional analysis by two way ANOVA revealed significant influence of *Toxoplasma-*

Table 1: ***Characteristics of Toxoplasma infected and Toxoplasma free healthy volunteers.***

	Toxoplasma seronegative				Toxoplasma seropositive			
Gender[a]	N	Mean	SD	%	N	Mean	SD	%
Males	41			82.0	9			18.0
Females	50			76.9	15			23.1
Total	91			79.1	24			20.9
Age[b]	91	27,4	6,5		24	31.2	8.9	
Education[c]								
Elementary	5			5.5	1			4.2
Vocational Secondary	4			4.4	1			4.2
General Secondary	60			65.9	13			54,1
College	2			2.2	3			12.5
University	20			22.0	6			25.0

[a] Pearson's chi-square 0.4410; p = 0.5066. Mann-Whitney chi-square 0.4454; p = 0.5044
[b] p = 0.021 in ANOVA
[c] Pearson's chi-square 5.1934; p = 0.2680. Mann-Whitney chi-square 4.1828; p = 0.3818

-seropositivity /F (1,111) = 5.43; p = 0.02/ but no influence of gender /F (1,111) = 1.75; p = 0.19/.

Discussion and conclusion

The present study is the first to present CPT performance results analysing overall toxoplasma infection effect. Is it reasonable to expect that latent infection with *T. gondii* could have an effect on human behavior (Flegr, 2007) and its results may contribute to the explanation of the increased incidence of traffic accidents in toxoplasma infected population (Flegr et al., 2002). The presented attention/vigilance analysis of healthy subjects sample is a first step to research the function of postnatal latent toxoplasmosis as a factor of vulnerability or symptom modifier in schizophrenia in the context of CNS project in Prague Psychiatric Center. In our study 1) we have verified that the seroprevalence of our sample correlate with the Prague general population one (20–30%) (Kodym et al., 2000); 2) We extended our knowledge of parasite-induced attention/vigilance changes: previous study (Havlíček et al., 2001) showed there is a tendency to increase the computerised simple reaction time in the 2nd to 3rd minute in *Toxoplasma*-positive healthy subjects. Coincidentally, we found gradual improvement of attention/vigilance performance in the course of 14 minutes test in infected individuals. It is important to note that the average mean reaction time in *Toxoplasma*-positive sample is non-significantly worse (T-score: 46.2) than in the *Toxoplasma*-negative one (T-score: 45.9). Even though our results show progressive improvement in reaction times over the testing time, one can argue that the slightly worse average performance in *Toxoplasma*-positive sample may suggest that *Toxoplasma*-positive subjects' cognitive efficiency is deteriorated in first minutes of the CPT test. Because the vigilance decrement occurs predominantly at the beginning of the test we may hypothesize some initial adjustment or performance

Table 2: ***Student's t test comparing CPT results in toxoplasma positive and toxoplasma negative samples.***

Parameter (T-scores in CPT)	Toxo - average	Toxo + average	t	Df	p	Number Toxo -	Number Toxo +	SD Toxo -	SD Toxo +
Age	27,37363	31,1667	-2,34709	113	0,020661	91	24	6,48014	8,90855
CPT omission	50,39582	51,1396	-0,32807	113	0,743469	91	24	8,81811	13,23980
CPT commission	52,47593	54,6338	-0,86384	113	0,389506	91	24	10,30534	12,90847
Hit Reaction Time	45,85813	46,2271	-0,21032	113	0,833794	91	24	7,49094	8,21856
Hit Reaction Time SE	44,61220	45,4900	-0,49282	113	0,623099	91	24	7,87367	7,31009
Variability of SE	46,24681	47,2196	-0,51585	113	0,606965	91	24	8,44253	7,27265
Attentiveness (d')	52,70516	53,3842	-0,30781	113	0,758792	91	24	8,92479	11,93065
Response Style	48,93648	49,2921	-0,16824	113	0,866695	91	24	8,38153	11,91425
Perseverations	50,42670	50,7350	-0,11837	113	0,905982	91	24	11,67873	9,95921
Hit Reaction Time Block Change	47,31560	51,8396	-2,70138	113	0,007969	91	24	7,14626	7,86435
Hit Standard Error Block Change	48,08418	49,9258	-0,88819	113	0,376325	91	24	8,89201	9,57899
Hit Reaction Time ISI Change	44,64374	45,9008	-0,66011	113	0,510526	91	24	8,18071	8,74685
Hit SE ISI Change	48,37934	48,4413	-0,03109	113	0,975249	91	24	9,02376	7,15760

T-score – represents the score of the individual taking the test relative to the population average and compares the respondent to those in the normative group who are of the same gender and who are in the same age group. Age groups are broken down by 6-7, 8-9, 10-11, 12-13, 14-15, 16-17, 18-34, 35-54, and 55+. T-score is a standard score with a mean of 50 and a standard deviation of 10. A T-score of 60 represents a score that is 1 standard deviation above the mean.

CPT omission – the number of targets to wich the individual did not respond**CPT commission** – the number of times the individual responded to a nontarget ("X")

Hit Reaction Time – the mean response time (in milliseconds) for all target responses over all six time blocks

Hit Reaction Time Standard Error – express the consistency of response times and variability of reactions

Variability of Standard Error – response time consistency: the standard deviation of the 18 standard error values calculated for each sub-block

Attentiveness (d') – the measure of discrimination between targets and nontargets and of the difference between the signal (non-X) and noise (X) distribution

Response Style – higher values reflect response style where individuals want to made sure they are correct and the emphasis is on avoiding commission errors.

Hit Reaction Time Block Change (vigilance measure) – the slope of change in reaction times over the six time blocks. A high T-score indicates quicker reaction times as the test progressed.

Hit Standard Error Block Change – the slope of change in reaction time standard errors over the six time blocks. A high T-score indicates that reaction times became less consistent as the test progressed.

Hit Reaction Time Inter-Stimulus Interval (ISI) Change – A high T-score indicates a slowing or reaction time as the time between targets increased (ISI: 1, 2, and 4 seconds).

Hit Standard Error ISI Change – is calculated by computing the slope of change in reaction time standard errors over the three ISIs (1, 2, and 4 seconds).

Toxo +: toxoplasma-infected, Toxo -: toxoplasma-free subjects

warm-up pattern impairment. 3) It has been reported that older drivers are able to compensate for the prolongation of their reaction times (Petridou, Moustaki, 2000). It suggests that the capacity for long-term concentration is more critical with respect to the risk of traffic accident. A retrospective case-control study carried out by Flegr et al. (2002) showed a significantly higher seroprevalence in the traffic accident participants. Initial decrease of attentional capacity may account for increased risk to be involved in a traffic accident. Here, we may speculate whether subjects with long-term parasitosis develop the ability to adjust their behaviour to the decrease of their psychomotor performance (Flegr et al., 2002) and some new adaptive strategies to deal with long-life attentional problems that manifests as gradual improvement in the course of CPT test. 4) Despite some findings showing TG infection results in decreased novelty seeking behaviour (Skallová et al., 2006) we did not find any differences in cognitive style, impulsivity and tendency to risk in TG-infected subjects. Limitation of this study is small sample size to perform more thorough analysis (the effect of Rh factor and gender) and the reliance on just antibody measurements. Additionally, results may be limited because long-term effects were not addressed. It is possible that the effects of the parasite are not due to the manipulation in an evolutionary sense but merely due to neuropathological or neuroimmunological effects of the parasite's presence. The results obtained during the past 15 years strongly suggest that latent toxoplasmosis influences the behaviour not only in rodent hosts but also in humans. The neurophysiological mechanisms and practical effects of these behavioral changes, however, are still to be elucidated (Flegr, 2007). Therefore, further research should be also focused on TG strains, host genes, cytokine production, individual genetic predisposition, the state of the immune system, the dose, the virulence of the infecting strain, the timing of infection, and the part of the brain affected (Torrey and Yolken, 2003).

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REFERENCES

Boronow J, Dickerson F, Stallings C, Lee B, Origoni A, Yolken R. HSV-1, CMV and Toxoplasma serology predict cognitive deficits in schizophrenia [abstract]. Schizophr Res 2002; 53:85.

Conners CK, Epstein JN, Angold A, Klaric J. Continuous Performance Test Performance in a Normative Epidemiological Sample. Journal of Abnormal Child Psychology. New York: 2003; 31:555.

Dickerson F, Boronow J, Stallings C, Origoni A, Yolken R. Toxoplasma gondii in individuals with schizophrenia: association with clinical and demographic factors and with mortality. Schizophr Bull 2007;33,3:737–740.

Flegr J, Hrdy I. Influence of chronic toxoplasmosis on some human personality factors. Folia Parasitol. 1994; 41:122-126.

Flegr J, Zitková S, Kodym P, Frynta D. Induction of changes in human behaviour by the parasitic protozoan Toxoplasma gondii. Parasitology 1996; 113:49-54.

Flegr J, Havlicek J. Changes in the personality profile of young women with latent toxoplasmosis. Folia Parasitol 1999; 46:22-28.

Flegr J, Hrdá Š, Havlíček J. Rozdíly v osobnostním profilu biologů nakažených a nenakažených T. gondii. Remedia Klin Mikrobiol 1999.

Flegr J, Kodym P, Tolarova V. Correlation of duration of latent Toxoplasma gondii infection with personality changes in women. Biological Psychology 2000; 53:57-68.

Flegr J, Havlicek J, Kodym P, Maly M, Smahel Z. Increased risk of traffic accidents in subjects with latent toxoplasmosis: a retrospective case-controlstudy, Bmc Infectious Diseases 2002; 2:1-6.

Flegr J, Preiss M, Klose J, Havlíček J, Vitáková M, Kodym P. Decreased level of psychobiological factor novelty seeking and lower intelligence in men latently infected with the protozoan parasite Toxoplasma gondii Dopamine, a missing link between schizophrenia and toxoplasmosis? Biological Psychology 2003; 63:253-268.

Flegr J. Effects of Toxoplasma on Human Behavior. Schizophrenia Bulletin 2007;.33, no.3:757-760.

Green DM, Swets JA. Signal detection theory and psychophysics. New York: Wiley. 1966.

Gros U. Toxoplasma gondii research in Europe. Parasitology Today 1996;12:1-4.

Havlíček J, Gasova Z, Smith AP, Zvara K, Flegr J. Decrease of psychomotor performance in subjects with latent ‚asymptomatic' toxoplasmosis, Parasitology 2001; 122:515-520.

Holliman RE. Toxoplasmosis, behavior, and personality. J Infect 1997;35:105-110.

Holub D, Motlová L, Rodriguez M, Dragomirecká E, Preiss M, Čermák J, Ungrmanová M, Nechutná R, Kaňková Š. Postnatal latent toxoplasmosis in schizophrenia: Cognitive and psychopathological correlates. Psychiatrie 2006; 10 (Suppl. 3): 66-70.

Holub D, Motlová L, Rodriguez M, Preiss M, Čermák J, Libiger J. Toxoplasma gondii u schizofrenie. Psychiatrie 2006;10(2): 81-87.

Ho-yen Do. Clinical features. In: Ho-yen Do, Joss AW, eds. Human Toxoplasmosts. Oxford: Oxford University Press, 1992: 57-78.

Kodym P, Malý M, Svandová E, Lekatková H, Badoutová M, Vlková J, Benes C, Zástera M. Toxoplasma in the Czech Republic 1923-1999: first case to widespread outbreak. Int J Parasitol 2000; 30:11-18.

Novotná M, Hanusova J, Klose J, Preiss, Havlicek J, Roubalová K, Flegr J. Probable neuroimmunological link between Toxoplasma and cytomegalovirus infections and personality changes in the human host. BMC Infectious Diseases 2005, 5:54.

Petridou E, Moustaki M. Human factors in the causation of road traffic crashes. Europ J Epidemiol 2000, 16:819-826.

Remington JS, Krahenbuhl J. Immunology of Toxoplasma gondii. In Immunology of

Human Infection, Part II (ed. Nahmias, AJ and O'Reilly J.), 1982;327-371. Plenum Publishing Corporation, New York.

Riccio CA., Reynolds CR, Lowe PA. Clinical applications of continuous performance tests. New York: Wiley. 2001.

Skallová A, Novotná M, Kolbeková P, Gašová Z, Veselý V, Sechovská M, Flegr J. Decreased level of novelty seeking in blood donors infected with Toxoplasma. Neuroendocrinology Letters 2005;26:480-486.

Tenter AM, Heckeroth AR, Weiss LM. Toxoplasma gondii: from animals to humans. Int J Parasitol. 2000;30:1217-1258.

Torrey EF, Yolken RH. Toxoplasma gondii and schizophrenia, Emerging Infectious Diseases 2003; 9:1375-1380.

Vavřinová R. Vliv latentní toxoplazmózy matky na postnatální vývoj potomků. Diplomová práce. 2005:51-56.

Yereli K, Balcioglu IC, Ozbilgin A. Is Toxoplasma gondii a potential risk for traffic accidents in Turkey? Forensic Sci Int. 2006;163:34-37.