ORIGINAL ARTICLE

Higher perceived dominance in *Toxoplasma* infected men – a new evidence for role of increased level of testosterone in toxoplasmosis-associated changes in human behavior

Hana Hodková, Petra Kolbeková, Anna Skallová, Jitka Lindová & Jaroslav Flegr

Department of Parasitology, Faculty of Science, Charles University in Prague, Czech Republic

Correspondence to: Dr. Jaroslav Flegr
Dept. of Parasitology, Faculty of Science, Charles University in Prague,
Vinicná 7, CZ-128 44 Prague 2, CZECH REPUBLIC
PHONE: +420-221951824
FAX: +420-224919704
EMAIL: flegr@cesnet.cz

Submitted: 2007-03-12 *Accepted: 2007-03-20*

Key words: **human; parasite; masculinity**

Neuroendocrinol Lett 2007; **28**(2):110–114 **PMID:** 17435678 NEL280207A02 © 2007 Neuroendocrinology Letters **www.nel.edu**

Abstract

Toxoplasma is parasite of cats that uses any warm-blooded animals as intermediate hosts. It is known to induce shifts in behavior, physiology and even morphology of its intermediate hosts, including humans. The lower second to fourth digit ratio (2D:4D ratio) in infected man and women, and higher height in infected man suggest that sex steroid hormones like testosterone could play a role in these shifts. Here, we searched for another indirect indication for a higher postnatal testosterone level, i.e. increased perceived dominance and masculinity in infected men. We showed portrait pictures of 89 male students of which 18 were *Toxoplasma*-infected to 109 female students. When we statistically corrected for age, men with latent toxoplasmosis were perceived as more dominant (p=0.009) and masculine (p=0.052). These results support the idea that the higher level of testosterone could be responsible for at least some of the toxoplasmosis-associated shifts in human and animal behavior.

INTRODUCTION

Toxoplasma gondii, an intestinal coccidian parasite of cats with a broad spectrum of intermediate hosts, is a very common human parasite, which usually infects 10–60% of inhabitants of various countries [39]. Infection in an early stage of pregnancy has often serious impacts on the health of infected infants, including microcephaly and hydrocephaly [17]. Infection in later stages of pregnancy usually results in less serious health impacts, such as sight and hearing defects [39]. Postnatally acquired toxoplasmosis in immunocompetent subjects causes mild disease, acute toxoplasmosis, and turns spontaneously into life-long latent toxoplasmosis, which is characterized by the presence of dormant stages of the parasite in cysts mostly in the neural and muscular tissues, and immunity against new *Toxoplasma* infections [15,29]. Latent toxoplasmosis in men is considered as clinically asymptomatic [23,31]. It is, however, accompanied by behavioral changes [9,10,13,19]. The behavioral alterations in the infected hosts, such as higher activity and lower psychomotor performance of *Toxoplasma*-infected

mice, are usually interpreted as a result of manipulative activity of the parasite aiming to increase the chance of transmission of the parasite from intermediate to definitive hosts [1,2,42]. Recently, it was also reported that latent toxoplasmosis increases the probability of birth of a son from 0.51 to 0.72 [16]. The personality changes observed in infected subjects, namely the tendency of infected men to disregard society rules [10,13], and the increased sex ratio in offspring of infected women [16], as well as oppositely directed shifts in most of the affected personality factors in men and women [13,19] suggest that altered levels of sex steroid hormones could play a role in certain toxoplasmosis-associated phenomena.

Supporting this hypothesis are two indirect indices of increased levels of steroid hormones in subjects with latent toxoplasmosis. First, infected men are taller and height is associated with higher concentration of testosterone [7]. Secondly, infected men and women have a lower second-to-fourth finger ratio (length index finger divided by the length of the ring finger), also called 2D:4D ratio [11] and a low 2D:4D ratio is associated with higher concentration of sex steroid hormones [21]. However, 2D:4D ratio reflects mainly the concentration of prenatal steroid hormones [22] while *Toxoplasma* infection should be related rather to postnatal concentration of the hormone. The problem with postnatal concentration of steroid hormones, especially testosterone, also is that it fluctuates widely during the season and during the day [4,5] and in response to different external stimuli [3]. This fluctuation makes it impossible to estimate long-term concentration of testosterone based on a one-shot measurement [33]. Indeed, there is usually no relation between the 2D:4D ratio and postnatal testosterone concentration [25].

Therefore, we searched for an independent marker of the long-term average testosterone level that would reflect the postnatal rather than prenatal concentration of testosterone. One such marker could be perceived dominance and masculinity [25], a complex of traits developed in men for the most part in puberty under strong influence of testosterone. Perceived dominance is hard to quantify objectively but can be easily estimated from photographical portraits by women raters [27].

In the present study we tested the testosterone hypothesis of toxoplasmosis-associated behavioral changes by searching for differences in perceived dominance and masculinity between *Toxoplasma*-infected and *Toxoplasma*-free male students.

METHODS

Subjects

Undergraduate biology students of the Faculty of Sciences, Charles University, Prague, were addressed during regular biology lectures and were invited to participate in the study on a voluntary basis. Eighty-nine (89) male students, mean age 21.2 years, SD=1.85, enrolled in the study and signed an informed consent form. All participants provided 2 ml of blood for serological testing and agreed to have a colour photograph of their face taken (Nicon Coolpix 4500, 4 Mega Pixels, distance 1.5 m, standard light conditions, frontal view, neutral facial expression) for the purposes of the study. The recruitment of the study subjects and data handling practices complied with the Czech regulations in force.

Serology

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 [28], 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 [41]. Titres of antibodies to *Toxoplasma* in the sera were measured at dilutions between 1:8 and 1:1 024. The subjects testing IgM negative by ELISA (positivity index<0.9) and having CFT titres higher than 1:8 were considered latent-toxoplasmosis positive.

Perceived dominance and masculinity rating

One hundred nine women raters, students of other faculties (aged 21–24), were individually invited for rating the photographs. Every woman rated the whole set of 89 photos (printed in format 9 × 12 cm), first for perceived dominance and then for masculinity on a seven point scale. The order of the photographs was randomised for each woman. In case a woman knew or was acquainted (even by sight) with a man in the picture, she was instructed not to rate that picture. The ratings of each woman were converted to z-scores to eliminate influence of individual differences between women, and perceived dominance and perceived masculinity was calculated for each man as his average z-score.

Statistics

The relation between perceived dominance and *Toxoplasma* infection was tested with General Linear Models (GLM) and with nonparametric Kendall tests. The statistical significance of the corresponding nonparametric tests was approximately the same, therefore we present here only the results of the GLM analysis in which the control for confounding factors (e.g. the age) is more straightforward.

RESULTS

Of the 89 men 18 (22%) were *Toxoplasma*-positive. The pictures of these men received higher perceived dominance scores (average z-score = 0.184) and masculinity scores (average z-score = 0.171) than the 71 *Toxoplasma*-free subjects (average z-scores of –0.057 and –0.030, respectively), Figure 1. The results of GLM tests showed that the difference was nearly significant for perceived dominance, ($F_{1,87} = 3.94$, p=0.051) but was not significant for masculinity ($F_{1,87} = 1.91$, p=0.170). When

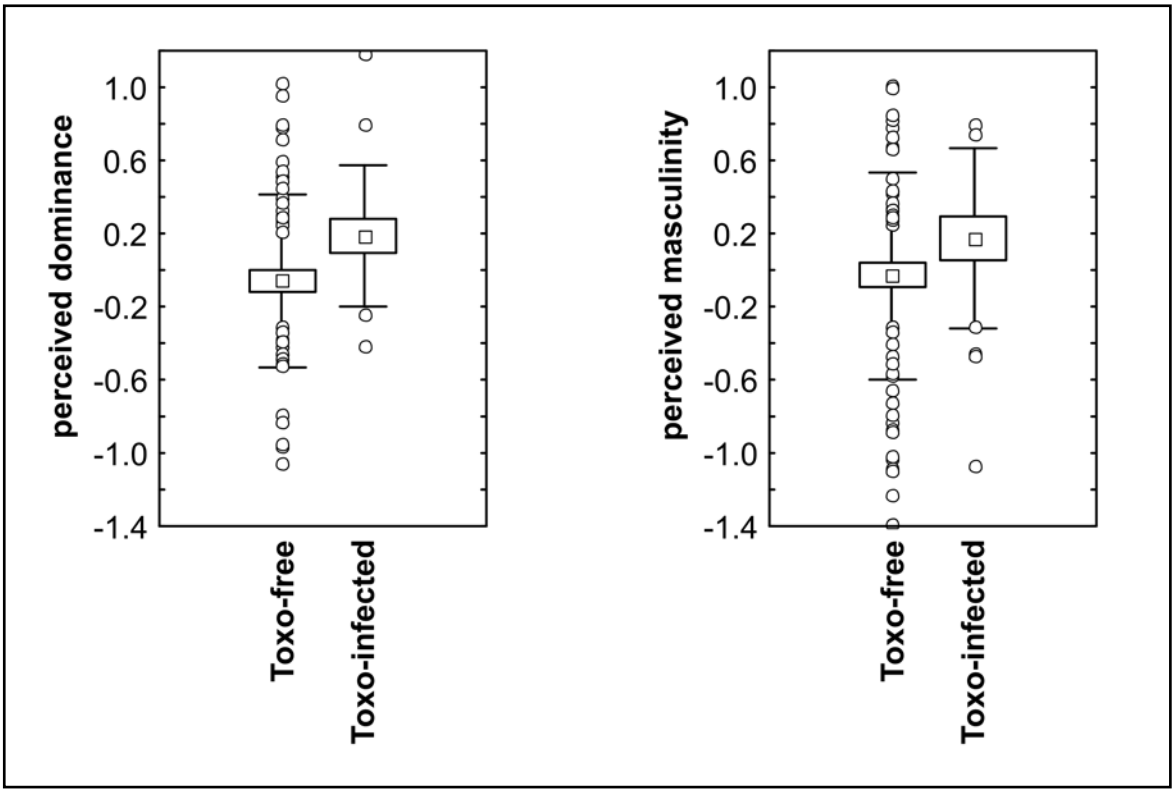

Figure 1. Difference in perceived dominance (left) and masculinity (right) between *Toxoplasma*-infected and *Toxoplasma*-free male students. The dominance and masculinity are expressed in z-scores, the small squares, boxes, whiskers and circles denote means, standard errors, standard deviations and outliers, respectively.

age (the trait positively correlated with perceived dominance and masculinity) was included into the model as a covariate, the difference in perceived dominance appeared highly significant ($F_{1,86}=7.04$, p=0.009) while that in masculinity was nearly significant ($F_{1,86}=3.87$, p=0.052). Composite photographs (Figure 2) made up of photographs of the 18 *Toxoplasma*-infected men (b) and of a random sample of photographs of 18 *Toxoplasma*-free men (a) illustrate the difference between these two groups.

DISCUSSION

Higher perceived dominance (and masculinity) of *Toxoplasma*-infected subjects was in accord with our hypothesis that *Toxoplasma*-infected subjects have higher levels of testosterone. Previous indirect indices of a higher testosterone level, i.e. a lower 2D:4D ratio in infected men and women and higher body height in infected men [11], were obtained for the same population of university students, therefore the present data cannot be considered as an independent evidence for the testosterone hypothesis. However, the relation between toxoplasmosis and perceived dominance remained approximately the same (in fact, it slightly increased) when the 2D:4D ratio was controlled for (not shown). This means that the effects of toxoplasmosis on the 2D:4D ratio and perceived dominance are independent (i.e. some *Toxoplasma*-infected men have both decreased 2D:4D ratio and increased perceived dominance but some have either decreased 2D:4D ratio or increased perceived dominance). Therefore, our results provide a new indirect support for the assumption that testosterone may be implicated in the personality and behavioral differences between *Toxoplasma*-infected and *Toxoplasma*-free subjects.

The testosterone hypothesis of toxoplasmosis-associated behavioral shifts does not specify whether subjects with a higher testosterone level are more prone to *Toxoplasma* infection or whether the increased testosterone level is a result of *Toxoplasma* infection. Here, we used a cross-sectional design, and therefore we cannot decide between these two possibilities. At face value, the lower 2D:4D ratio in *Toxoplasma*-infected subjects (a feature supposedly formed during the early embryonic stage) supports the former hypothesis while the higher perceived dominance of infected men (a trait that reflects the testosterone level at the adolescent age) is rather consistent with the latter one. However, it must be kept in mind that prenatal and postnatal testosterone levels could be correlated [36]. Therefore, subjects with higher perceived dominance (and with higher postnatal testosterone levels) are also more likely to have higher prenatal testosterone levels (and therefore a lower 2D:4D ratio). Moreover, the recently published data suggest that the

Copyright © 2007 Neuroendocrinology Letters ISSN 0172–780X • www.nel.edu

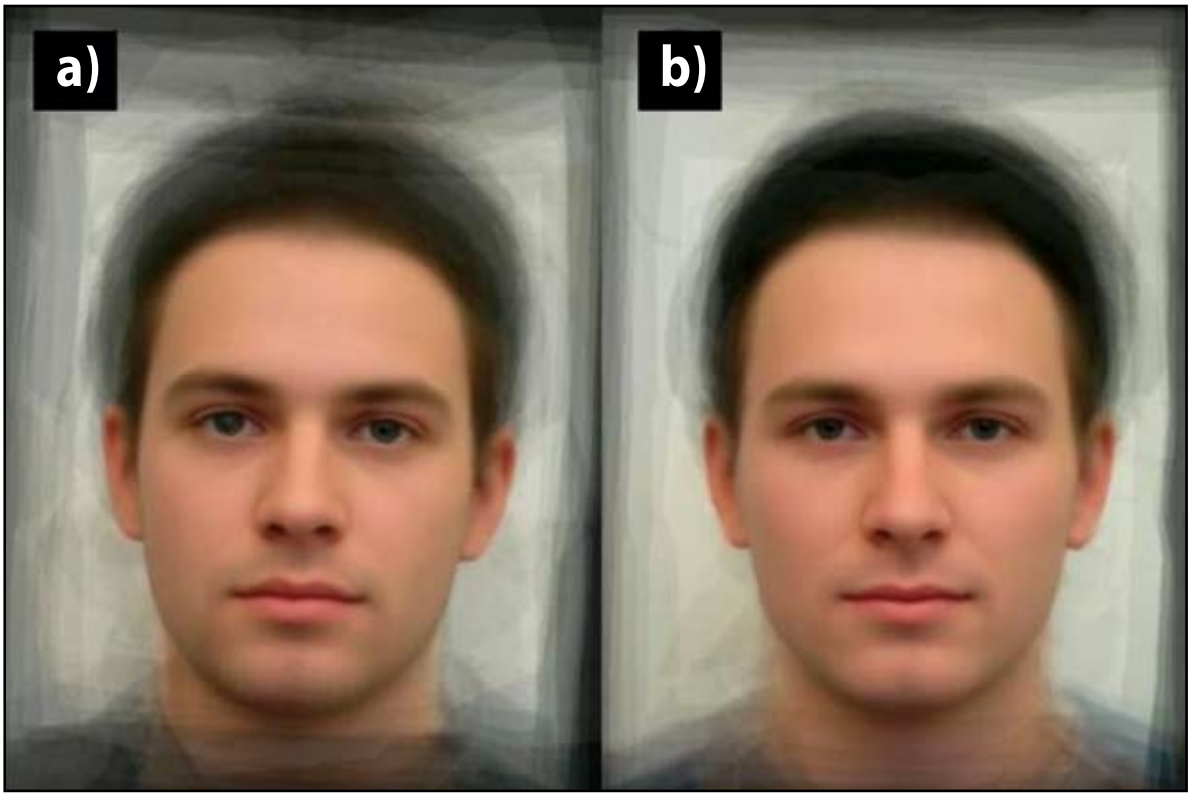

Figure 2. Composite photographs of 18 Toxoplasma-free (a) and 18 Toxoplasma-infected students (b)
(In all reported tests, the original photographs of students, and not these composite photographs, were rated.)

2D:4D ratio varies during postnatal life and therefore, at least theoretically, could be influenced by (toxoplasmosis induced) increased testosterone levels [24,40]. It might indicate that perceived dominance, as well as several other psychological traits [8,20] is related to the 2D:4D ratio for the right hand, while toxoplasmosis is associated with a lower left hand 2D:4D ratio. One possible explanation of this pattern, rather speculative indeed, could be that the right hand 2D:4D ratio reflects more the prenatal testosterone levels, while the left hand 2D:4D ratio is rather linked to postnatal testosterone levels (and thus is more prone to be influenced by environmental factors, including *Toxoplasma* infection).

Toxoplasma gondii is known to manipulate the behavior [9,10,13,19] and sex ratio [16] of its hosts (rodents, under natural conditions), thus possibly increasing the probability of its transmission to definitive hosts, the cats. There are both indirect and direct indices that dopamine plays an important role in the observed behavioral changes in rodents [34,37] and possibly also in humans [12,26,35]. The increased testosterone level could be either a product of increased dopamine level [6,14,38]] or a second independent mechanism of manipulation of the intermediate host's behavior. Testosterone may also be a byproduct of other, possibly pathogenic, activities of the parasite in the body of infected hosts or may be involved in the manipulation of the host immune response. It is known that high concentrations of steroid hormones have immunosuppressive effects [30,32] and some parasitic species, e.g. *Taenia crassiceps,* can manipulate the level of these hormones to increase their chance of surviving in the hostile environment of the host body [18].

At present, three independent lines of evidence, i.e. a lower 2D:4D ratio, higher body height and higher perceived dominance, suggest that *Toxoplasma* infected men have a higher level of testosterone. Unfortunately, all three lines are only indirect. In the future, it is critically needed to obtain direct (biochemical) evidence of increased testosterone levels in infected men. Moreover, the testosterone hypothesis deals with proximate mechanism of behavioral changes observed in *Toxoplasma*-infected subjects. To reveal the causality relations between the toxoplasmosis and testosterone, it will be important to measure testosterone concentrations in experimentally infected laboratory animals to show whether elevated testosterone levels are a consequence of infection or only increase the chance of acquiring *Toxoplasma* infection.

ACKNOWLEDGEMENTS

We thank to A. C. Little for help with preparing illustrative composite photographs and A. Kuběna for his statistical advice. The study was supported by grants No. 406/07/0581 of the Grant Agency of the Czech Republic and No. 0021620828 of the Czech Ministry of Education.

REFERENCES

1 Barnard CJ, Behnke JM. Parasitism and Host Behaviour. Taylor and Francis, New York. 1990.
2 Berdoy M, Webster JP, Macdonald DW. Fatal attraction in rats infected with *Toxoplasma gondii*. Proc R Soc London, B Biol Sci. 2000; **267**: 1591–1594.
3 Bernhardt PC, Dabbs JM, Fielden JA, Lutter CD. Testosterone changes during vicarious experiences of winning and losing among fans at sporting events. Physiol Behav. 1998; **65**: 59–62.
4 Dabbs JM. Age and seasonal-variation in serum testosterone concentration among men. Chronobiol Int. 1990; **7**: 245–249.
5 Dabbs JM. Salivary Testosterone measurements – reliability across hours, days, and weeks. Physiol Behav. 1990; **48**: 83–86.
6 Dominguez JM, Hull EM. Dopamine, the medial preoptic area, and male sexual behavior. Physiol Behav. 2005; **86**: 356–368.
7 Drop SLS, De Waal WJ, Keizer-Schrama SMPF. Sex steroid treatment of constitutionally tall stature. Endocrine Reviews. 1998; **19**: 540–558.
8 Fink B, Neave N, Manning JT, Grammer K. Facial symmetry and the 'big-five' personality factors. Pers Indiv Differ. 2005; **39**: 523–529.
9 Flegr J, Havlicek J, Kodym P, Maly M, Smahel Z. Increased risk of traffic accidents in subjects with latent toxoplasmosis: a retrospective case-control study. BMC Infect. Dis. 2002; **2**: art-11.
10 Flegr J, Hrdy I. Influence of chronic toxoplasmosis on some human personality factors. Folia Parasitol. 1994; **41**: 122–126.
11 Flegr J, Hruskova M, Hodny Z, Novotna M, Hanusova J. Body height, body mass index, waist-hip ratio, fluctuating asymmetry and second to fourth digit ratio in subjects with latent toxoplasmosis. Parasitology. 2005; **130**: 621–628.
12 Flegr J, Preiss M, Klose J, Havlicek J, Vitakova 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? Biol Psychol. 2003; **63**: 253–268.
13 Flegr J, Zitkova S, Kodym P, Frynta D. Induction of changes in human behaviour by the parasitic protozoan *Toxoplasma gondii*. Parasitology, 1996; **113**: 49–54.
14 Hull EM, Muschamp JW, Sato S. Dopamine and serotonin: influences on male sexual behavior. Physiol Behav. 2004; **83**: 291–307.
15 Jones JL, Kruszon-Moran D, Wilson M, McQuillan G, Navin T, Mcauley JB. *Toxoplasma gondii* infection in the United States: Seroprevalence and risk factors. Am J Epidemiol. 2001; **154**: 357–365.
16 Kanková Š, Šulc J, Nouzová K , Fajfrlík K, Frynta D, Flegr J. Women infected with parasite *Toxoplasma* have more sons. Naturwissenschaften. 2007; **94**: 122–127.
17 Koppe JG, Rothova A. Congenital toxoplasmosis. A long-term follow-up of 20 years. Int Ophthalmol. 1989; **13**: 387–390.
18 Larralde C, Morales J, Terrazas I, Govezensky T, Romano MC. Sex hormone changes induced by the parasite lead to feminization of the male host in murine *Taenia crassiceps* cysticercosis. J Steroid Biochem Mol Biol. 1995; **52**: 575–580.
19 Lindová J, Novotna M, Havlicek J, Jozífkova E, Skallova A, Kolbekova P, Hodny Z, Kodym P, Flegr J. Gender differences in behavioural changes induced by latent toxoplasmosis. Int J Parasitol. 2006; **36**: 1485–1492.
20 Luxen MF, Buunk BP. Second-to-fourth digit ratio related to verbal and numerical intelligence and the big five. Pers Indiv Differ. 2005; **39**: 959–966.
21 Manning JT. Digit ratio: A pointer to fertility, behavior, and heatlh. Rutgers University Press, New Jersey. 2002: 1–173 pp.
22 Manning JT, Scutt D, Wilson J, Lewis-Jones DI. The ratio of 2nd to 4th digit length: a predictor of sperm numbers and concentrations of testosterone, luteinizing hormone and oestrogen. Hum Reprod. 1998; **13**: 3000–3004.
23 Markell EK, John DT, Krotoski WA. Markell and Voge's Medical parasitology. W.B. Saunders Company, Philadelphia, 1999.
24 McIntyre MH, Ellison PT, Lieberman DE, Demerath E, Tone B. The development of sex differences in digital formula from infancy in the Fels Longitudinal Study. Proc R Soc London, B Biol Sci. 2005; **272**: 1473–1479.
25 Neave N, Laing S, Fink B, Manning JT. Second to fourth digit ratio, testosterone and perceived male dominance. Proc R Soc London, B Biol Sci. 2003; **270**: 2167–2172.
26 Novotna M, Hanusova J, Klose J, Preiss M, Havlicek J, Roubalova K, Flegr J. Probable neuroimmunological link between *Toxoplasma* and cytomegalovirus infections and personality changes in the human host. BMC Infect Dis. 2005; **5**.
27 Penton-Voak IS, Chen JY. High salivary testosterone is linked to masculine male facial appearance in humans. Evol Hum Behav. 2004; **25**: 229–241.
28 Pokorny J, Fruhbauer Z, Polednakova S, Sykora J, Zastera M, Fialova D. Stanoveni antitoxoplasmickych protilatek IgG netodou ELISA (Assessment of antitoxoplasmatic IgG antibodies with the ELISA method). Cs Epidem. 1989; **38**: 355–361.
29 Remington JS, Krahenbuhl JL. Immunology of *Toxoplasma gondii*. In Nahmias,AJ, O'Reilly,J (Eds.). Immunology of human infection, Part II Plenum Publishing Corporation, New York.1982, pp. 327–371.
30 Roberts LS, Janovy JJr, Gerald S Schmidt & Larry S. Roberts' Foundations of parasitology. McGraw-Hill Companies, Inc, Boston, 2000.
31 Roberts LS, Janovy JJr , Gerald S Schmidt & Larry S Roberts' Foundations of parasitology. McGraw-Hill Companies. Inc, Boston. 2000.
32 Schuster JP, Schaub GA. Experimental Chagas disease: the influence of sex and psychoneuroimmunological factors. Parasitol Res. 2001; **87**: 994–1000.
33 Shirtcliff EA, Granger DA, Likos A. Gender differences in the validity of testosterone measured in saliva by immunoassay. Horm. Behav. 2002; **42**: 62–69.
34 Skallova A, Frynta D, Kodym P, Flegr J. The role of dopamine in *Toxoplasma*-induced behavioural alterations in mice: an ethological and ethopharmacological study. Parasitology. 2006; **133**: 525–535.
35 Skallova A, Novotna M, Kolbekova P, Gasova Z, Vesely V, Flegr J. Decreased level of novelty seeking in blood donors infected with toxoplasma. Neuroendocrinol Lett. 2005; **26**: 480–486.
36 Sorenson JC, Meier RJ, Campbell BC. Dermatoglyphic asymmetry and testosterone levels in normal males. Am J Phys Anthropol. 1993; **90**: 185–198.
37 Stibbs HH. Changes in brain concentrations of catecholamines and indoleamines in *Toxoplasma gondii* infected mice. Ann Trop Med Parasitol.1985; **79**: 153–157.
38 Szczypka MS, Zhou QY, Palmiter RD. Dopamine-stimulated sexual behavior is testosterone dependent in mice. Behav Neurosci. 1998; **112**: 1229–1235.
39 Tenter AM. Heckeroth AR, Weiss LM. *Toxoplasma gondii*: from animals to humans. Int J Parasitol. 2000; **30**: 1217–1258.
40 Trivers R, Manning J, Jacobson A. A longitudinal study of digit ratio (2D : 4D) and other finger ratios in Jamaican children. Horm Behav. 2006; **49**: 150–156.
41 Warren J, Sabin AB. The complement fixation reaction in toxoplasmic infection. Proc Soc Exp Biol Med. 1942; **51**: 11–16.
42 Webster JP. The effect of *Toxoplasma gondii* and other parasites on activity levels in wild and hybrid *Rattus norvegicus*. Parasitology. 1994; **109**: 583–589.

Copyright © 2007 Neuroendocrinology Letters ISSN 0172–780X • **www.nel.edu**