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An exploratory study of long-term neurocognitive outcomes following recovery from opportunistic brain infections in HIV+ adults

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Abstract

Central nervous system opportunistic infections (CNS-OI) are a significant cause of morbidity and mortality in AIDS. While current interventions are increasingly successful in treating CNS-OI, little information exists regarding long-term behavioral outcomes among survivors. In this exploratory study we examined neurocognitive data among three groups of adults with different AIDS-related CNS-OI: 15 with past cryptococcal meningitis (CM), 8 with toxoplasmosis encephalitis (TE), and 8 with progressive multifocal leukoencephalopathy (PML). A group of 61 individuals with AIDS, but without CNS-OI, was used as a comparison group. A battery of standardized neuropsychological tests assessing a variety of cognitive domains was administered upon entry. Results indicate that individuals with a history of CNS-OI were most impaired on measures of cognitive and psychomotor speed relative to the HIV+ comparison group. Among the CNS-OI groups, individuals with history of TE had the most severe and varied deficits. The results are discussed in relation to what is known about the neuropathological consequences of the various CNS-OIs. While this is the first systematic group study of residual CNS-OI effects on neurocognitive function, future studies employing more participants, perhaps focusing on specific CNS-OIs, will further characterize the long-term outcomes in AIDS-related CNS-OI.

Keywords

Opportunistic infection; AIDS; Neuropsychological functioning; Toxoplasmosis encephalitis; Progressive multifocal leukoencephalopathy; Cryptococcal meningitis

Since its introduction in 1996, highly active antiretroviral therapy (HAART) has, when used in combination with adjunctive and prophylactic antibiotic therapy, dramatically decreased the incidence of central nervous system opportunistic infections (CNS-OI) and has improved the longevity of people with AIDS (Collier et al., 1999; Neuenburg et al., 2002; San-Andreas et al., 2003). HAART has also contributed to improved survival among those AIDS patients who develop a CNS-OI (Kirk et al., 2002). These conditions, which at one time typically resulted in death, can now be treated. Further, while HIV infection itself may lead to neuropathological changes, the CNS-OIs common among AIDS patients often result in more severe structural brain lesions. Currently, little information exists regarding the long-term cognitive and functional outcomes in individuals who survive AIDS-related CNS-OIs. For example, do most survivors of AIDS-related CNS-OI recover to such a degree that they can return to work or independent living? Examination of the changes in survivors' neuropsychological abilities is necessary to understand the benefits and limitations of current treatments, to identify obstacles in returning affected individuals to independence, and to plan for their long-term care.

Individuals with AIDS are vulnerable to a number of CNS-OIs. Among the most common are toxoplasmosis encephalitis (TE), caused by the parasite *Toxoplasmosis gondii*, cryptococcal meningitis (CM) caused by the fungus *Cryptococcus neoformans*, and progressive multifocal leukoencephalopathy (PML), caused by the JC papovavirus (JCV). There is a paucity of studies examining the long-term neurocognitive and functional outcomes of those who survive. In one such study, 8 individuals with AIDS/PML were followed for a median of 44 months (Gasnault et al., 1999). Despite no change in overall group neurological status between baseline and the study end, case-by-case analysis revealed that 1 participant had worsened, while 4 improved, and 3 remained unchanged. More recently, another group reported on the progress of two AIDS patients who survived PML (Wyen, Lehmann, Fatkenheuer, & Hoffman, 2005). One, a 50-year-old man when diagnosed with PML, still had neurologic deficits (hemiparesis) 8 years later, although his other deficits had subsided, and brain lesions had diminished to an extent. However, the neurologic deficits in their other patient, a 26-year-old man, had completely resolved after just 8 months, and after 13 months he had resumed full-time work. While comprehensive neurobehavioral assessment was not reported for these individuals, the findings indicate that there may be individual characteristics that determine recovery from CNS-OI and give hope that some of those who survive PML can recover enough neurologically to function independently once again. Recently, Paul et al. (2007) examined an HIV+ individual with PML at baseline and again one year later using diffusion tensor imaging and neuropsychological measures. They found that this individual had greater neurocognitive impairment and white matter fiber loss than did two HIV+ individuals without PML.

In the current study, we examined neuropsychological data among an ethnically diverse cohort of adults diagnosed with one of the three AIDS-related CNS-OIs described above. Our goal was to understand the long-term impact of these conditions. To our knowledge, this is the first study of the long-term neuropsychological outcomes among a relatively large group of individuals with AIDS-related CNS-OI.

Method

Participants

All participants were enrolled in the National Neurological AIDS Bank (NNAB). The NNAB is a longitudinal study funded by the National Institutes of Health and is approved by the University of California, Los Angeles (UCLA) Medical Institutional Review Board. Using the standardized data collected by NNAB, we examined neurological and neuropsychological data collected from NNAB participants. A total of 92 male and female participants with AIDS, chosen from a sample of over 400 NNAB participants, were included in the current study and were placed into either the AIDS-related CNS-OI or a comparison group composed of HIV-

infected participants without a history of CNS-OI. All individuals were taking HAART upon study entry. A total of 15 individuals were diagnosed with definite CM, 8 with definite TE, and 8 with PML (4 had probable PML and 4 definite PML). The remaining 61 participants were included as a comparison group. Individuals in the latter group had AIDS, generally due to low nadir CD4+ cell count (<200) or non-CNS-OI, but did not have a history of CNS-OI or HIV-related neurocognitive disorder.

Inclusion/exclusion criteria—All participants or their legal guardians were required to sign an institutional review board (IRB)-approved informed consent before entry. Criteria for inclusion into the general NNAB study are as follows: HIV-1 infection documented by antibody test, Western Blot, and/or polymerase chain reaction (PCR); age at least 18 years; any gender; willingness and ability to give informed consent (or has a legal guardian who can do so); resides within 120 miles of Los Angeles, CA, at enrollment; and meets one or more of the following criteria at study entry: (a) an absolute CD4+ cell count of 50 cells/mm³ or less; (b) a CNS complication of AIDS, such as AIDS dementia; (c) one or more major systemic opportunistic infections or a malignant tumor; (d) heart failure; (e) a serum albumin of less than 3.2 g/dl; (f) renal failure; or (g) any other medical condition that in the opinion of the study physician is likely to lead to death within the next 2 years.

AIDS-related CNS-OI group members were selected for the current study as follows: (a) They had a complete study visit, including neurological and neuropsychological examinations, a psychiatric interview, and urine toxicology screening for drugs of abuse, and (b) they met the criteria (described below) for one of three AIDS-related CNS-OIs: TE, CM, or PML. Participants were deemed ineligible for the current analysis if they had more than one CNS-OI (such as TE and CM), had a confounding medical or neurological condition that impaired cognition (including hepatic encephalopathy, seizure disorder, stroke, or major head trauma), or had any of the following disorders: HIV-associated dementia, HIV-associated minor cognitive/motor disorder, neurosyphilis, learning disability (per self-report), and/or current substance dependence per the Psychiatric Research Interview for Substance and Mental Disorders (Hasin, Trautman, & Endicott, 1998). Autopsy-confirmed diagnosis of CNS-OI was available for a subset of participants who had expired while participating in the NNAB study. Presence or absence of a systemic opportunistic disease (such as *Pneumocystis carinii* pneumonia,) did not affect inclusion into the study. Participants in the comparison group also met the criteria for a history of AIDS, had no history, signs, or symptoms of a CNS-OI, and no evidence of HIV-associated dementia or other neurocognitive disease as described above. The comparison group was matched to the CNS-OI groups according to age, education, and viral load. Participants whose neurological diagnosis was so confounded by one or more variables such as acute systemic illness with fever, metabolic encephalopathy, or severe psychiatric illness such that the etiology of their deficits could not be ascribed to a CNS-OI were not included in the current study.

Diagnostic criteria for the CNS-OI

TE: A diagnosis of possible TE required (a) enhancing brain mass lesion(s) and (b) positive toxoplasma immunoglobulin G (IgG)titer. A diagnosis of probable TE required that the participant met criteria for possible TE and a definite response by clinical or imaging improvement to drugs with known activity against *Toxoplasma gondii*. A diagnosis of definite TE required a brain biopsy showing unequivocal histological evidence of toxoplasma organisms in an inflamed area of brain.

CM: A diagnosis of definite CM required a history of new neurological symptoms or fever and identification of *Cryptococcus neoformans* in cerebrospinal fluid by one or more of the following methods: India ink stain, cryptococcal antigen, or fungal culture. In addition, workup

revealed no other organisms in cerebrospinal fluid (CSF) or brain. Probable CM was diagnosed if meningitis due to *Cryptococcus neoformans* was strongly suspected (as in the case of a meningitis that accompanied a proven pulmonary infection), but not proven because of a failure to obtain cerebrospinal fluid, a failure of laboratory processing of cerebrospinal fluid, or use of antifungal therapy, which may have interfered with the diagnosis.

PML: A diagnosis of possible PML required a new focal neurological disturbance(s) and imaging findings on contrast-enhanced brain scan consistent with PML, and that confounding illnesses (i.e., other CNS diseases capable of producing the clinical syndrome) were present, or available information was not sufficient to rule out confounding illnesses. The diagnosis of possible PML was also made in cases where the clinical and magnetic resonance imaging (MRI) findings were consistent with PML, but a test for JCV in CSF performed more than 6 months after the acute illness was negative. A diagnosis of probable PML required appropriate clinical and radiographic findings consistent with PML, and the patient had no other illness that could explain the clinical picture. A diagnosis of definite PML was made if appropriate clinical and radiological findings were present, and either (a) JCV PCR was positive in CSF or (b) a brain biopsy was diagnostic for PML. All of the participants in the CNS-OI groups entered the study in a nonacute phase; that is, they had survived a well-documented AIDS-related CNS-OI.

Procedure

Upon study entry participants were administered a comprehensive battery of psychometric measures assessing neuropsychological ability, substance abuse, and depression. These data were collected by two psychometrists trained by a board-certified neuropsychologist and certified by the NNAB Neuropsychology Quality Assurance Committee.

Neuropsychological battery—Trail Making Test (Army Individual Test Battery, 1944), Hopkins Verbal Learning Test–Revised (Brandt, 1991), Brief Visuospatial Memory Test–Revised (Benedict, Schretlen, Groninger, Dobraski, & Shpritz, 1996), Paced Auditory Serial Addition Test–Trial 1 (Gronwall, 1977), Wisconsin Card Sorting Test–64 Card Version (Kongs, Thompson, Iverson, & Heaton, 2000), Grooved Pegboard (Klove, 1963), Controlled Oral Word Association Test (Benton & Hamsher, 1989), and three subtests from the Wechsler Adult Intelligence Scale, 3rd Edition (Wechsler, 1997)—Digit Symbol Test, Symbol Search, and Letter Number Sequencing. Raw scores were transformed into T-scores using normative data contained with the test manuals for the Wechsler subtests, Hopkins Verbal Learning Test–Revised, and Brief Visuospatial Memory Test–Revised. For all other measures, published normative data were used (Heaton, Grant, & Matthews, 1991). The neuropsychological tests were grouped into the following neurocognitive domains: processing speed, attention/working memory, learning, memory, verbal fluency, abstraction, and motor speed. Measures comprising these domains are shown in Table 1. In addition, a global measure of cognitive functioning was obtained that collapsed functioning across all of these domains. Scores of tests within each domain were averaged to produce the domain T-score, and all test scores were averaged to produce the global T-score.

Psychiatric illness—The substance use disorders and affective disorders modules of the Psychiatric Research Interview for Substance and Mental Disorders (Hasin et al., 1998), were administered to all participants at study entry. Psychometric properties of this instrument were previously reported to be very good with this population (Morgello et al., 2006).

Neurological diagnoses—Standardized neurological examinations, lumbar punctures, and a review of the participant's medical records were performed by one of three board-certified study neurologists with extensive experience in neuroAIDS. Neurological diagnoses were arrived at via consensus agreement between the examining neurologist and neuropsychologist,

with consideration of lab results (blood, urine toxicology, and CSF), neuroimaging, and medical history, using a structured set of algorithms. The diagnosis of a current or treated CNS-OI was determined at study entry based on the data.

Statistical analysis

As an initial analysis, the groups were compared with regards to demographic characteristics and disease variables (e.g., viral load and length of infection) using analysis of variance (ANOVA) and chi-square (Table 2). Neuropsychological functioning was then compared between the comparison group and three CNS-OI groups, with any significantly discrepant demographic variables entered as covariates. The Tukey honestly significantly different (HSD) test was used for post hoc analyses.

Results

The groups did not differ statistically with regard to age, $F(3, 88)=0.46, p=.71$, education, $F(3, 88)=0.73, p=.54$, or mean viral load, $F(3, 66)=0.69, p=.56$. Length of HIV infection was significantly different, $F(3, 88)=4.48, p < .01$. Post hoc analysis showed that the CM group had significantly shorter length of infection than did the comparison group, by an average of 5.5 years ($p < .01$). Proportions of females ($\chi^2=7.01, p=.07$), current major depression ($\chi^2=8.04, p=.53$), ethnic representation ($\chi^2=13.84, p=.31$), and proportion of individuals who were primarily Spanish speaking ($\chi^2=7.01, p=.07$) were statistically similar among the comparison and CNS-OI groups. Only the comparison group contained females, who made up approximately 20% of that group.

Neuropsychological comparisons between the groups are presented in Table 3. ANOVAs were significant for all neuropsychological domains. Post hoc analyses showed that this was generally driven by the large discrepancies between the comparison group's scores and those of the various CNS-OI groups. On all but the memory domain, it was the TE group that had significantly lower scores than the comparison group. Relative to the comparison group, PML group had significantly lower scores on the speed of information processing and motor domains, while the CM group had lower scores on the verbal fluency and motor domains.

It was possible that the scores observed for the TE group were artificially deflated due to the large number of primary Spanish speakers in that group (Jacobs et al., 1997; Lyness, Hernandez, Chui, & Teng, 2006). To examine this, we performed independent samples *t* tests for each of the cognitive domains, using language (Spanish vs. English) as the grouping variable. There were 4 Spanish speakers and 4 English speakers in the TE group. None of the *t* tests were statistically significant (see Table 4).

Discussion

In this exploratory study, we examined the long-term neuropsychological outcomes in individuals with a history of AIDS-related CNS-OI, including TE, CM, and PML. To our knowledge, this is the first systematic group study of residual CNS-OI effects on neurocognitive function in HIV+ individuals. Our observations suggest that these conditions leave most individuals with a poor prognosis regarding recovery of cognitive functioning. Characterizing the deficits in these individuals could lead to targeted rehabilitation and possibly improve prognosis and return to independence.

Upon study entry, all three CNS-OI groups had poorer neuropsychological functioning than did HIV+ individuals who did not have a history of AIDS-related CNS-OI, despite the fact that the latter group had been infected with HIV for an equal or longer duration. Those with past TE appeared to have the poorest neuropsychological functioning across all but the memory

domain, and this was not attributable to the large number of primary Spanish speakers in that group. The CM group differed from the comparison group on the verbal fluency and motor domains, while the PML group differed on the information processing and motor domains. More so than the other domains, these consisted of measures given under the pressure of time, in which scores were time dependent. Thus, it may be that the AIDS-related CNS-OIs examined here result in persistent deficits of cognitive and psychomotor processing speed. Notably, such deficits have historically been among the most commonly observed in HIV+ individuals, even those considered asymptomatic (Arendt & von Giesen, 2002; Davis, Skolasky, Selnes, Burgess, & McArthur, 2002; Dunlop et al., 2002; von Giesen, Haslinger, Rohe, Köller, & Arendt, 2005). Thus, these AIDS-related CNS-OIs may serve to potentiate HIV-related deficits in psychomotor and cognitive processing speed. Conversely, the deficits may exist as a consequence particular to these conditions.

Aside from these deficits, which were consistent across AIDS-related CNS-OIs in our cohort, it is unlikely that these conditions are associated with a distinct neuropsychological profile, as they can affect the entire brain or large portions within. For example, toxoplasmic tachyzoites, the cause of TE, multiply rapidly in the brain cells that they parasitize and give rise to a strong inflammatory reaction and diffuse brain lesions in grey and white matter (Falangola, Reichler, & Petito, 1994). TE thus results in a variety of focal neurological deficits, brain edema, and increased intracranial pressure. Survivors of TE may be afflicted with any number of problems, including hydrocephalus, permanent focal motor and sensory deficits, or seizures (Arendt et al., 1999). PML causes severe demyelination associated with lysis of oligodendrocytes, as well as axonal loss, and focal neurological deficits such as hemiparesis (Roberts, 2005). And while most cases of CM preferentially involve the meninges, AIDS patients may develop focal abscesses (cryptococcomas) within the brain parenchyma (Lee, Dickson, & Casadevall, 1996), and CM can result in increased intracranial pressure, strokes, brain abscess, and parenchymal loss (Bicanic & Harrison, 2004; Woodworth, McGirt, Williams, & Rigamonti, 2005). The effects of the lesions caused by these CNS-OIs on neurobehavioral functioning varies widely. CM has been associated with mania (Johannessen & Wilson, 1988), TE has been found to mimic HIV-associated dementia (Arendt et al., 1991) and to be associated with alexia (Luscher & Horber, 1992), and PML has been associated with integrative agnosia (Butter & Trobe, 1994). Thus, these conditions can result in focal or generalized neuropsychological abnormalities, as well as alterations in psychiatric functioning. This is supported by the case studies described earlier (Gasnault et al., 1999; Paul et al., 2007; Wyen et al., 2005), in which there were vastly differing long-term outcomes in individuals with PML. In sum, it appears from our results, as well as previous findings, that aside from decreased cognitive and psychomotor processing speed, these infections may not be associated with distinct neuropsychological profiles, but instead with a wide range of neurologic and psychiatric impairments. In those with HIV, it may also be increased severity of deficits rather than a distinct profile.

To our knowledge, these findings are drawn from the largest cohort of individuals with a history of AIDS-related CNS-OI to date. However, the conclusions are tentative due to a number of limitations. First, information regarding the dates of AIDS-related CNS-OI was not available. As a result, it is not known how much time had passed since the acute phase of the illnesses. Such information will be valuable in the future, as it will allow trajectory of recovery to be ascertained. The recent findings reported by Paul et al. (2007) provide a promising methodology (i.e., diffusion tensor imaging) for such studies; however, larger sample sizes will be required. A second limitation is the limited power due to small sample sizes. Fortunately, the small CNS-OI group sizes likely reflect the efficacy of antiretroviral treatment. However, they are also the result of rather stringent inclusion criteria used for the present study. Individuals were excluded who had current substance use disorders and history of a wide variety of neurologic disorders and complications. Substance use is quite common in our cohort

and typical of the HIV+ population in the greater Los Angeles area. Finally, it can be argued that our decision to exclude individuals with HIV-associated neurocognitive disorders resulted in an inflated difference of neuropsychological scores between the comparison and CNS-OI groups. However, in this exploratory study we wished to characterize the deficits in the CNS-OI groups, which was possible only by comparing them to a similar group of individuals that differed only on the presence or history of an AIDS-related CNS-OI. For future studies, in which the long term functional and real-world outcomes of CNS-OIs are examined, the inclusion of individuals with HIV-related cognitive deficits will be important.

To conclude, we have presented data indicating that HIV+ individuals with a history of CNS-OI continue to have severe and lasting neuropsychological impairments as compared to HIV + individuals with no history. Studies employing more participants, as well as functional measures of day-to-day functioning, are required to further advance our understanding of the long-term consequences of AIDS-related CNS-OI.

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TABLE 1

Neuropsychological measures comprising the cognitive domains

Domain	Measure
Information processing	Symbol Search, Digit Symbol, Trail Making Test–Form A
Learning	Hopkins Verbal Learning Test–Revised (Learning Trials 1–3), Brief Visuospatial Memory Test–Revised (Learning Trials 1–3)
Memory	Hopkins Verbal Learning Test–Revised (Recall Trial), Brief Visuospatial Memory Test–Revised (Recall Trial)
Abstraction	Wisconsin Card Sorting Test–Perseverative Responses, Trail Making Test–Form B
Verbal fluency	Controlled Oral Word Association Test
Attention/working memory	Letter–Number Sequencing, Paced Auditory Serial Addition Test–Trial 1
Psychomotor	Grooved Pegboard (both hands)

TABLE 2

Group characteristics

Variable	CM (n=15)	TE (n=8)	PML (n=8)	Comparison (n=61)	p-value
Age (years) ^a	39.6 (9.1)	42.8 (7.1)	42 (7)	42.4 (8.6)	.71
Education (years) ^a	12.3 (4.1)	12.6 (3)	14.3 (2.7)	13.1 (2.8)	.54
Viral load	1,700	3,386	400	3,930	.56 ^c
Estimated length of HIV infection (years) ^a	4.6 (3.7)	7 (4)	10.4 (7.9)	10.1 (5.7)	.01
Gender (% male) ^b	100	100	100	80.3	.07
Current depression ^b	18.2	20	0	16.3	
Primary language (% Spanish) ^b	40	50	0	14	.07
Ethnicity					.31
Caucasian ^b	80	75	75	57.4	
Native American ^b	6.7	0	0	13.1	
African American ^b	6.7	12.5	25	27.9	
Mixed ^b	6.7	12.5	0	0	

Note. CM=cryptococcal meningitis. TE=toxoplasmosis encephalitis. PML=progressive multifocal leukoencephalopathy.

^a Means; standard deviations in parentheses.

^b Percentages of participants in each group.

^c Viral load analysis of variance (ANOVA) based on mean values for each group.

TABLE 3

Neuropsychological functioning

Domain	Group	Mean	SD	SE	95% confidence intervals		F	p-value	Effect size ^d	Group differences
					Lower	Upper				
Global	Comparison	46.0	9.1	1.2	43.6	48.3	7.27	>.001	.18	Comp > all CNS-OI
	TE	33.2	7.9	2.8	26.6	39.8				
	PML	36.2	13.1	4.6	25.3	47.2				
	CM	38.3	10.1	2.6	32.7	43.8				
Information processing speed	Comparison	47.9	8.2	1.1	45.8	50.0	7.71	>.001	.19	Comp > PML, TE
	TE	37.5	11.7	4.1	27.7	47.6				
	PML	32.3	15.4	5.4	19.4	45.1				
	CM	47.9	14.4	3.7	32.9	48.8				
Learning	Comparison	42.7	11.2	1.4	39.8	45.6	4.20	.01	.11	Comp > TE
	TE	28.8	9.0	3.2	21.3	36.2				
	PML	42.4	11.8	4.2	32.5	52.3				
	CM	36.7	13.0	3.4	29.5	43.9				
Memory	Comparison	43.2	10.7	1.4	40.5	46.0	3.37	.02	.2	
	TE	31.9	11.5	4.3	21.3	42.5				
	PML	44.5	10.2	3.6	35.0	53.0				
	CM	36.5	13.6	3.5	29.0	44.0				
Abstraction	Comparison	46.7	7.8	1.0	44.7	48.9	5.71	.001	.15	Comp > TE
	TE	33.6	6.7	2.4	28.0	39.2				
	PML	37.6	18.1	6.4	22.4	52.7				
	CM	41.5	13.9	3.7	33.5	49.5				
Verbal fluency	Comparison	48.3	8.7	1.1	46.1	50.5	7.28	>.001	.17	Comp > CM, TE
	TE		35.4	13.6	4.8	24.0				
	PML	39.1	12.4	4.4	28.8	49.5				
	CM	40.3	9.3	2.4	35.1	45.4				
Attention/working memory	Comparison	45.5	8.1	1.0	43.5	47.6	3.66	.02	.1	Comp > TE
	TE		35.8	6.5	2.3	30.4				
	PML		44.9	10.2	3.6	36.4				
						53.5				

Domain	Group	Mean	SD	SE	95% confidence intervals		F	p-value	Effect size ^a	Group differences
					Lower	Upper				
Psychomotor	CM	41.2	10.5	2.7	35.4	47.0				
	Comparison	41.0	10.6	1.4	38.3	43.7	10.87	>.001	.26	Comp > all CNS-OI
	TE	28.1	12.5	4.4	17.7	38.6				
	PML	21.5	6.9	2.4	15.7	27.3				
	CM	32.1	12.9	3.3	25.0	39.2				

Note. Presented as *t*-scores, with lower scores indicating poorer performance. CM=cryptococcal meningitis. TE=toxoplasmosis encephalitis. PML=progressive multifocal leukoencephalopathy.

^aEffect size estimated by partial eta squared.

TABLE 4

English versus Spanish speakers in TE group

Domain	English (n=4)	Spanish (n=4)	F	p-value
Global	34.4 (10.4)	32 (5.9)	0.16	.7
Information processing	39.3 (13.9)	35.7 (10.9)	0.17	.7
Learning	33.3 (11.2)	24.3 (2.8)	2.4	.17
Memory	37 (12.9)	25.2 (5.1)	2.2	.2
Abstraction	33.1 (8.1)	34 (6.2)	0.03	.87
Verbal fluency	32.8 (17.6)	38 (10.2)	0.27	.63
Attention/working memory	33.9 (5.5)	37.8 (7.6)	0.68	.44
Psychomotor	29.1 (13.4)	27.1 (13.4)	0.04	.84

Note. Means, with standard deviations in parentheses. TE=toxoplasmosis encephalitis.