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Selective attention function impairment in HIV-negative patients with early forms of neurosyphilis

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Abstract

Background The attentional network test (ANT) is widely used to evaluate the performance of three attentional networks: alerting, orienting and executive attention networks. This study aimed to investigate the characteristics of attention functions in HIV-negative patients with early forms of neurosyphilis (NS) and their correlation with abnormalities in brain magnetic resonance imaging (MRI).

Methods Thirty patients with early forms of NS, 31 patients with syphilis but without NS (Non-NS) and 35 healthy controls were recruited from an HIV-negative cohort between September 2020 and November 2022. The participants were evaluated with the ANT and the Mini-Mental State Examination (MMSE). Brain MRI was performed in NS and Non-NS patients.

Results No significant differences were observed in the MMSE scores among the three groups. However, patients with early forms of NS showed poorer performance in orienting and alerting functions than Non-NS group ($F=6.952$, $P=0.011$ and $F=8.794$, $P=0.004$, respectively); No significant difference was observed in executive function between the two groups ($F=0.001$, $P=0.980$). Multivariate analysis of variance using the Bonferroni post hoc test indicated that patients with NS exhibited less efficient orienting function ($P=0.023$), and alerting function ($P=0.003$) but not executive function ($P=0.99$), compared to Non-NS patients. Additionally, a significant difference was found in orienting function between patients with NS and healthy controls ($P<0.001$) compared to healthy controls. MRI scans revealed that the NS group had a higher prevalence of abnormalities in the frontal lobes and/or the temporoparietal junction compared to the Non-NS group (24/25 vs. 13/19, $P=0.032$).

Conclusions The orienting and alerting functions but not executive function were significantly less efficient in early forms of NS group than in the Non-NS group ($P<0.01$). This indicates deficits in selective attention in patients with early forms of NS. Brain MRI scans revealed abnormalities in the frontal and/or parietal lobes, as well as the temporoparietal junction, suggesting potential neuropathological correlates of these attentional deficits.

Keywords HIV, Neurosyphilis, Attentional network test, Alerting, Orienting, Executive control

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Introduction

Neurosyphilis (NS) is caused by the invasion of central nervous system by *Treponema pallidum* subspecies *pallidum (T. pallidum)*, and it can occur at any stage of syphilis; NS is categorized into early and late forms of NS [1]. Late NS is routinely characterized by tabes dorsalis and general paresis [2, 3], while early forms of NS may present headache, meningismus, cranial nerve palsies, blindness, deafness, or it may be asymptomatic, characterized by abnormal laboratory results for cerebrospinal fluid (CSF) without any neurological findings [1, 4]. The clinical manifestations of NS are diverse and nonspecific, which poses a challenge to distinguishing early forms of NS from other conditions. Cognitive decline is a common manifestation of patients with late NS, particularly in those with general paresis, which is a progressive brain disease leading to both mental and physical deterioration. Most studies have focused on NS-related dementia, often neglecting mild or earlier cognitive impairment. Recently, NS-related mild cognitive impairment including executive and attentional functions impairment has been reported in limited studies [5, 6]. Nonetheless, the relationship between early forms of NS and cognitive impairment remains poorly understood.

Attention, as a pivotal part of cognition, is defined as the ability to allocate appropriate processing resources to relevant stimuli, discriminate preferential choices, and optimize performance toward behavioral goals, thereby enhancing overall cognitive efficiency and effectiveness [7]. According to the Attention Network Theory, proposed by Posner and Petersen, the attentional system is categorized into three independent networks: alerting, orienting, and executive functions. Each of these networks is associated with specific anatomical region and specific functions. The alerting network maintains a state of readiness and alertness to process stimuli, driven by norepinephrine and involves the thalamus, frontal cortex, and parietal cortex. The orienting network directs attention to specific locations or stimuli, influenced by acetylcholine and includes the parietal and frontal lobes, temporoparietal junction, pulvinar, and superior colliculus. The executive network manages high-level cognitive functions such as conflict resolution, planning, and decision-making, modulated by dopamine and involves the anterior cingulate cortex and lateral prefrontal cortex [8, 9].

The attentional network test (ANT) software, designed by Fan et al. [10], is a reliable and simple tool for assessing the function of the three attention networks. The ANT has been widely used to explore the detailed attentional characteristics in individuals with neuropsychiatric disorders, such as attention-deficit/hyperactivity disorder, schizophrenia, and Alzheimer's disease [11–13]; however, there is no existing research about the relationships between NS and the three attention networks. Studies on cognitive decline in patients with NS primarily utilized the Mini-Mental State Examination (MMSE) or the Montreal Cognitive Assessment (MOCA) to evaluate general or extensive cognitive impairment [14–16]. However, MMSE and MOCA are inadequate for detecting early cognitive impairment or cognitive impairment in specific domains. In addition to white matter hyperintensities in patients with general paresis which are associated with attention impairment [17], our previous studies [18, 19], revealed that patients with early forms of NS (asymptomatic NS and meningovascular NS) exhibit some degree of white matter demyelination. Thus, we hypothesized that patients with early forms of NS might also experience attention deficits. To investigate this hypothesis, we employed the ANT to investigate the potential attention function impairments in HIV-negative patients with early forms of NS and evaluate its association with imaging abnormalities.

Methods

Patient

We recruited all consecutive HIV-negative syphilis patients with NS or Non-NS who visited our hospital from September 2020 to November 2022. The diagnostic criteria for NS was based on Chinese sexually transmitted disease treatment guidelines [20]. and were as follows: (i) positive results for serum *T. pallidum* particle agglutination (TPPA) and toluidine red unheated serum tests (TRUST); (ii) CSF-TPPA reactivity; and (iii) CSF-TRUST positive or CSF white blood cell (WBC) count of ≥ 5 cells/μL or CSF protein concentration of > 50 mg/dL. No other diseases of CNS cause CSF pleocytosis or elevated protein. Furthermore, early forms of NS included asymptomatic NS, which is characterized by abnormal laboratory results on CSF without any neurological findings, or included symptomatic NS presenting with headache, meningismus, cranial nerve palsies, blindness or deafness [1]. Non-NS was defined as a seropositive result for TPPA and TRUST but a negative result for CSF-TRUST and CSF-TPPA [2]. All patients were diagnosed by two independent dermatologists and/or neurologists, and disagreements were resolved by consensus. The exclusion criteria were as follows: (i) HIV-positive patients; (ii) those who presented with signs of vision or hearing loss, late forms of NS (general paresis), or other conditions affecting cognitive function and cooperation; and (iii) an MMSE score of ≤ 24. A flowchart depicting the patient inclusion and exclusion criteria is presented in Fig. 1. Finally, 61 patients participated and completed both the MMSE and ANT. Among them, 55 patients received the recommended penicillin, one received oral doxycycline,

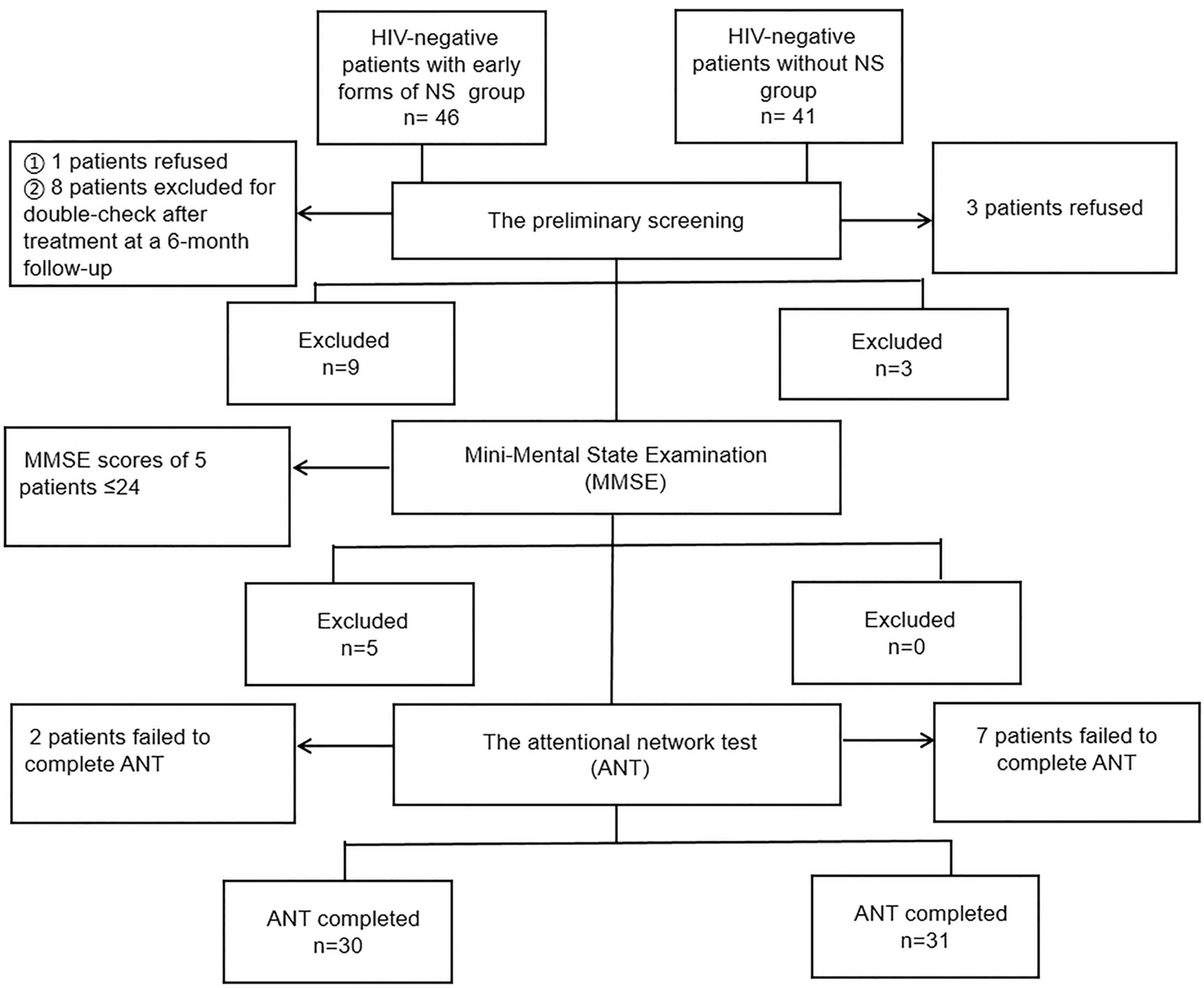

Fig. 1 Flowchart showing details of the participant flow in early forms of neurosyphilis and non-neurosyphilis groups

and another received ceftriaxone due to penicillin allergy, additionally, four patients were diagnosed with NS due to neurological symptoms, despite no prior history of syphilis infection. During the same period, healthy volunteers without *T. pallidum*, HIV infection or other central nervous system diseases were recruited as the control group; they also completed the MMSE and ANT assessments.

Clinical data collection

Clinical data of all participants, such as demographic characteristics, education levels, clinical symptoms and signs, serum and CSF-TRUST titers, CSF WBC count and protein levels, MMSE scores and ANT performance on admission, and brain MRI results during hospitalization, were collected.

The MMSE is a widely used screening scale that assesses cognitive functions, including orientation, memory, attention, language, and structure. This examination comprises an objective structured scale with 11 specific items and a total score of 30. There are different cutoff points based on education levels, and a score of ≤ 24 is defined as abnormal [21]. All scores were accurately assessed by trained physicians previously unaware of the patients' clinical diagnosis.

ANT

ANT, designed by Fan et al. [10], is a reliable and well-known tool for assessing attention deficit (Supplemental Fig. 1). Each trial begins by presenting a fixation cross in the middle of a computer screen. The stimulus signal—a warning cue (asterisk) or a target (arrow)—may appear above or below the center of the screen. Four cue conditions are present: (i) no cue, in which the fixation cross continues to appear at the first site; (ii) center cue, in which an asterisk appears at the central fixation cross; (iii) double cue, in which asterisks appear both above and below the central fixation cross; and (iv) spatial cue, in which an asterisk appears on the target location (either above or below the central fixation cross). Furthermore, three target conditions are present: (i) neutral target, in which there is only one central arrow; (ii) congruent target, in which there are five arrows in the same direction and the central arrow is the target; and (iii) incongruent target, in which the arrows flank the target point in the direction opposite to that of the central target arrow.

When the test starts, the eyes of the participants are 60 cm away from the screen, and they are instructed to fix their eyes on the cross throughout the test. Each trial includes five steps and lasts for 4000 ms. First, the fixation cross appears in the middle of the screen for 400–1600 ms. Second, the warning cue is presented for 100 ms. Third, the fixation cross appears for 400 ms. Fourth, the target is displayed for < 1700 ms. The participants must determine the direction of the target arrow by pressing the direction key in the keyboard as quickly and accurately as possible. Finally, the fixation cross appears in the middle of the screen again. The initial practice block comprised 24 trials, followed by three experimental blocks, and each block comprised 96 trials; thus, the entire test comprised 312 trials. The entire test session lasts approximately 30 min; however, pauses and rests are allowed between the blocks. The computer records the response time (RT) and accuracy during the process. All subjects finished the ANT on the same computer with a resolution of 1366*768 pixels and a screen size of 12.5 inches in this study.

The effects of the three attention networks were assessed using the differences in RTs [10]. The RTs of the three attention networks were calculated as follows:

$$RT_{\text{alerting effect}} = RT_{\text{no cue}} - RT_{\text{double cue}}$$
$$RT_{\text{orienting effect}} = RT_{\text{center cue}} - RT_{\text{spatial cue}}$$
$$RT_{\text{executive function effect}} = RT_{\text{incongruent}} - RT_{\text{congruent}}$$

Neuroimaging assessment

Brain MRI was performed on patients with and without NS, and the results were obtained by independent radiologists and further assessed by experienced radiologists who were unaware of the clinical diagnoses. The images were acquired using a 1.5- or 3.0-T system (Magnetom Avanto 1.5 T, Siemens, Berlin, Germany or Signa HDxt 3.0 T, GE Healthcare, Milwaukee, WI, USA), and all patients underwent axial plain scan without enhanced scan. The patients were placed in the supine position, and the head imaging plane was parallel to the line of the anterior and posterior union of the corpus callosum. A 1.5 T Siemens MRI scanning sequence was fast spin echo T1WI (TR 525 ms, TE 17 ms), T2WI (TR 3200 ms, TE 82 ms), fluid-attenuated inversion recovery (Flair) (TR 7500 ms, TE 122 ms), slice thickness 6 mm, spacing 3 mm, fast spin echo 18 cm*18 cm, matrix 256*230; and a 3.0 T GE MR scanning sequence was fast spin echo T1WI (TR 2000 ms, TE 24 ms), T2WI (TR 3380 ms, TE 102 ms), fluid-attenuated inversion recovery (TR 9000 ms, TE 120 ms) and diffusion-weighted imaging (DWI) (TR 5200 ms, TE minimum), slice thickness 6 mm, interval 1.5 mm, field of view 24 cm*24 cm, matrix 384*224.

Statistical analyses

The TRUST titers were $\log_2$ transformed ($\log_2 1$/TRUST titer) for analysis. Quantitative variables were presented as means ± standard deviations or medians (interquartile), as appropriate. One-way analysis of variance (ANOVA) or the Mann–Whitney U test was used to compare the quantitative variables, depending on the data distribution. The Chi-square test was used for qualitative variables. Multivariate ANOVA (MANOVA) was performed with the effects of the three attentional networks, mean RT, and overall accuracy as dependent variables among the three groups (i.e., patients with early forms of NS group vs. Non- NS group, patients with early forms of NS group vs. healthy controls; Non- NS group vs. healthy controls). To determine the possible association between the groups and the pattern of attention network function, MANOVA with Bonferroni post hoc test was performed, focusing on the effects of the three attentional networks, mean RT, and overall accuracy. Differences with two-sided P values of < 0.05 were considered statistically significant. Statistical analyses were performed using Statistical Package for the Social Sciences (version 19.0; IBM Corp., Armonk, NY, USA) and GraphPad Prism (version 5.01; GraphPad Software, San Diego, CA, USA).

Results

Baseline data

As shown in Fig. 1, 61 HIV-negative patients with syphilis were included in this study, comprising 30 patients with early forms of NS and 31 patients without NS (Non-NS). All patients and 35 healthy controls completed the study. Table 1 summarizes the demographic and clinical characteristics of patients with or without NS. Unlike the non-NS group, men were predominant in the NS group (14/30 vs. 6/31; $P = 0.03$). The mean age of the patients was higher in the NS group than that in the non-NS group (49.5 ± 12.4 vs. 37.6 ± 11.8 years; $P < 0.001$). The median serum-TRUST titers were significantly higher in the NS group than those in the non-NS group [1:16 (1:4, 1:32) vs. 1:1 (1:1, 1:4); $P < 0.001$]. CSF WBC count and CSF protein concentration were significantly higher in

Table 1 Demographic variables, clinical characteristics of patients with and without NS

Characteristics	NS (n = 30)	Non-NS (n = 31)	Statistics (NS vs. Non-NS)
Sex (male, %)	14 (46.7%)	6 (19.4%)	χ^2 = 5.161, P = 0.03
Age (years)	49.53 ± 12.39	37.65 ± 11.83	F = 14.696, P < 0.001
Age ≥ 45 years (n, %)	21 (70.0%)	7 (22.6%)	χ^2 = 13.805, P < 0.001
Education levels (years)	9.1 ± 3.00	9.8 ± 3.75	F = 0.721, P = 0.40
MMSE score	28.17 ± 1.74	29.00 ± 1.46	F = 2.666, P = 0.11
Serum-TRUST titers, (median, IQR)	1:16 (1:4, 1:32)	1:1 (1:1, 1:4)	Z = − 4.890, P < 0.001
CSF WBC count (106/L) (median, IQR)	7 (5, 13)	4 (3,4)	Z = − 4.222, P < 0.001
CSF protein level (mg/dL) (median, IQR)	39.72 (28.19, 55.84)	21.96 (15.02, 27.27)	Z = − 4.112, P < 0.001
Syphilis infection time (months) (median, IQR)	24 (12.00, 39.00)	36 (12.00, 60.00)	Z = − 1.802, P = 0.072

MMSE Mini-Mental State Examination, *serum-TRUST* serum toluidine red unheated serum test, *CSF* cerebrospinal fluid, *WBC* white blood cell, *NS* neurosyphilis, *IQR* interquartile range

the NS group than those in the non-NS group [7 (5, 13) vs.4 (3, 4) cells/μL, P < 0.001; 39.72 (28.19, 55.84) vs. 21.96 (15.02, 27.27) mg/dL, P < 0.001; respectively]. No differences were observed in education levels or MMSE scores or syphilis infection time between NS group and non-NS group (both P > 0.05).

Differences in attentional network effects among the groups

Figure 2 illustrates the interactions between different conditions for medians of RT in each group. In the distribution of the line chart, a difference in the performance was observed in the mean and standard deviation values of median RTs among the three groups under different cue or target conditions.

As shown in Table 2, significant differences in alerting (F = 8.794, P = 0.004) and orienting (F = 6.952, P = 0.011) effects and mean RT (F = 4.861, P = 0.031) were observed between the NS and the non-NS group. However, no significant differences were observed in executive effect (F = 0.001, P = 0.980) and overall accuracy between the two groups (F = 1.820, P = 0.183). Furthermore, the performance of the ANT was examined using a three-way MANOVA to compare the differences in RTs according to the syphilis infection groups (non-NS and NS), sex, and age (≤ 45 and > 45 years). There was neither a significant three-way multivariate interaction effect nor an interaction effect for sex ∗ syphilis infection groups and age group ∗ syphilis infection groups at the multivariate level. A significant main effect on RTs was observed for the infection group (P = 0.001). Moreover, Bonferroni post hoc test revealed that patients with NS exhibited less efficient orienting attention (P = 0.023) and alerting attention (P = 0.003) but not executive attention (P = 0.99) than patients without NS. No other significant differences were found between the two groups.

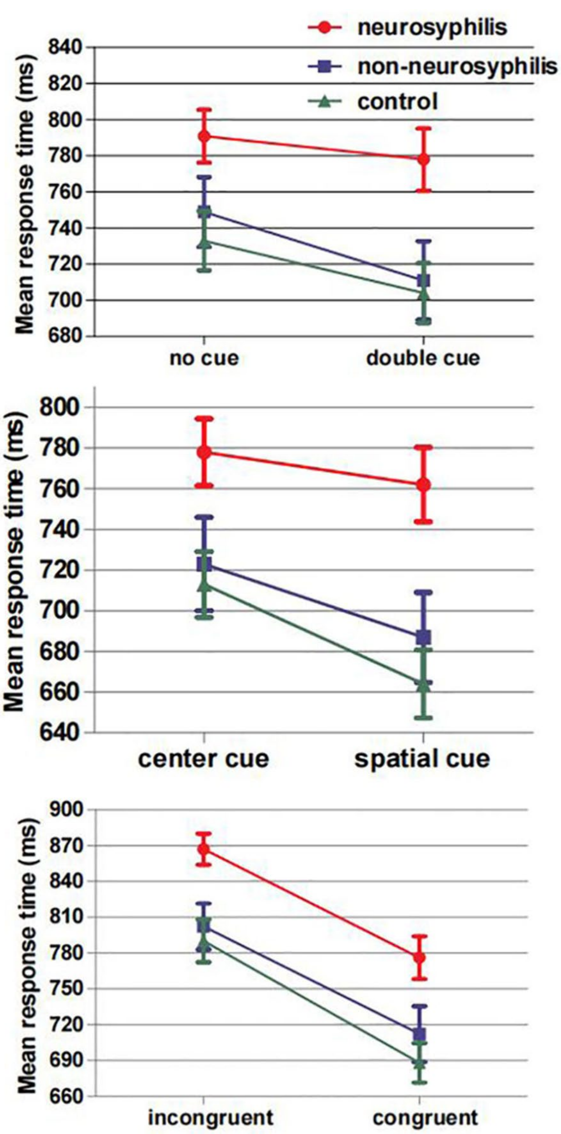

Fig. 2 The interactions between different conditions for medians of RT in each group

Table 2 Attentional network test response times and accuracy of patients with and without NS

Parameter	NS ($n=30$)	Non-NS ($n=31$)	Statistics
Alerting effect (ms)	13.10 ± 39.60	38.29 ± 25.45	F = 8.794, $P=0.004$
Orienting effect (ms)	16.57 ± 32.26	36.00 ± 24.96	F = 6.952, $P=0.011$
Executive effect (ms)	90.23 ± 68.72	89.87 ± 41.76	F = 0.001, $P=0.980$
Mean response time (ms)	777.37 ± 89.64	717.52 ± 119.70	F = 4.861, $P=0.031$
Overall accuracy (%)	90.53 ± 11.09	94.29 ± 10.66	F = 1.820, $P=0.183$

As shown in Supplemental Table 1, significant differences in orienting effect (F = 17.451, $P<0.001$), mean RTs (F = 13.378, $P=0.001$), and overall accuracy (F = 14.621, $P<0.001$) were revealed between patients with NS and controls. Moreover, a difference in overall accuracy was observed between patients without NS and controls (F = 4.427, $P=0.040$). Post hoc analysis using the Bonferroni method showed that patients with NS presented less efficient orienting attention than healthy controls ($P<0.001$). No significant differences in alerting and executive attention were found between NS and non-NS group and healthy controls (both $P>0.05$).

Comparison of neuroimaging between the groups

Overall, 25 patients with NS and 19 patients without NS underwent brain MRI. Table 3 shows the differences in neuroimaging between the NS and Non-NS groups, including white matter hyperintensity and lacunar infarction. No significant differences were noted in neuroimaging lesions involving the brain region alone (i.e., frontal, temporal, parietal, insular, and periventricular lobes) between the two groups (all $P>0.05$). However, the NS group had more patients with abnormalities in the frontal and/or parietal lobes and/or the temporoparietal junction than the non-NS group (24/25 vs. 13/19, $P=0.032$) (As shown in Supplementary Figs. 2, 3).

Discussion

In this study, the performance of the ANT was assessed for the first time among HIV-negative patients with early forms of NS compared to a Non-NS group, and healthy controls. Patients with early forms of NS exhibited poorer performance in orienting and alerting function compared to the Non-NS group and less efficient orienting function compared to healthy controls. However, no significant differences were observed in executive function among the groups. These findings suggest a selective impairment in attention functions particularly in orienting and alerting, in HIV-negative patients with early forms of NS.

Cognitive impairment, including alterations in attention, disorientation to time and place [16, 22]; and impairments in language, memory recall, and visuospatial abilities, and frontal executive functions [5], has been commonly reported in patients with late-stage NS, particularly those with general paresis. In contrast, it remains unclear whether attentional impairment occurs in patients with early forms of NS who do not exhibit detectable cognitive decline. The ANT has been validated as a sensitive tool for assessing attention function impairments, especially in the attentional networks, and is widely used in various conditions, including Alzheimer's disease, posterior circulation ischemia, and HIV-associated cognitive disorder [23–25]. This study highlights the benefit of the ANT in detecting cognitive impairment in patients with early forms of NS who maintain normal MMSE scores.

This study demonstrated that HIV-negative patients with early forms of NS had significantly shorter RTs compared to those without NS and healthy controls in tasks involving the orienting network. This suggests that these patients exhibit less efficient orienting attention functions after receiving target stimuli or locating targets. In

Table 3 Brain MRI characteristics of patients with and without NS

Abnormal neuroimagings	NS ($n=25$)	Non-NS ($n=19$)	P value
Frontal lobe	15 (60.0%)	7 (36.8%)	$\chi^2=3.191$, $P=0.074$
Parietal lobe	9 (36.0%)	6 (31.6%)	$\chi^2=0.094$, $P=1.0$
Temporal lobe	2 (8.0%)	2 (10.5%)	$\chi^2=0.083$, $P=1.0$
Periventricular lobe	6 (24.0%)	1 (5.3%)	$\chi^2=2.833$, $P=0.119$
Insular lobe	2 (8.0%)	1 (5.3%)	$\chi^2=0.127$, $P=1.0$
The frontal and/or parietal lobes and/or the temporoparietal junction	24 (96.0%)	13 (68.4%)	$\chi^2=6.138$, $P=0.032$

contrast, patients with early forms of NS showed similar response delays under both incongruent and congruent target conditions compared to healthy controls and those without NS, indicating that their executive attention function remains equally efficient. Additionally, there was a significant difference in alerting function between the NS and Non-NS groups, but not between the NS group and healthy controls. Previous studies have shown that age is associated with changes in alerting function [11, 26], and age was identified as a risk factor for HIV-negative patients with NS in our earlier research [27]. Therefore, we employed MANOVA with Bonferroni post hoc test to determine whether patients with NS still displayed less efficient orienting and alerting attention functions. The findings suggest that early forms of NS may be linked to specific structural impairments in the brain networks related to localization or alerting function rather than executive function.

The relationship between cognitive decline and cranial imaging abnormalities has been determined in patients with NS [5, 14]. Patients with NS presenting with ischemic stroke and a higher burden of cerebral small vessel disease showed reduced cognitive function, accompanied by progressive brain damage [14]. Gao et al. reported that in patients with general paresis, cerebral atrophy predominantly occurred in the anterior brain, and abnormal signals were distributed across various brain regions, primarily in the frontal and temporal lobe. These patients experienced impairments in delayed recall, visuospatial/executive and language ability, with the temporal lobe potentially being the first brain region affected [15]. A pilot single photon emission computed tomography (SPECT) study among HIV-negative patients with NS revealed perfusion abnormalities in the frontal, insular, and posterior cingulate regions, suggesting potential links between regional structure and cognitive deficits [28]. Our study found that patients with early forms of NS exhibited MRI abnormalities in the parietal lobes and/or frontal lobes, and/or the temporoparietal junction, correlating with impairments in orienting or/and alerting functions. Inflammation and the immune response related to intracranial *T. pallidum*-related may contribute to neural network impairment, leading to functional abnormalities in these lobes, mild cognitive decline, and dementia. The observed MRI abnormalities in these brain regions indicated a potential shift in the neural structures associated with them.

This study has several limitations. First, it focused on early forms of NS in participants from a single center, and the sample size was limited. This might have introduced selection bias. Second, although limited functional neuroimaging studies using SPECT or PECT/CT have adequately explored the association of cerebral perfusion, metabolic abnormalities, and cognitive decline, most have reported variable results. Further attentional assessment at additional time points, such as post-antisyphilis therapy, could provide better insights into post-treatment cognitive development, which is an important area for future studies.

Conclusions

HIV-negative patients with early forms of NS exhibited significant impairments in orienting and alerting attention functions. The ANT proved to be an effective tool in identifying these specific attention deficits in patients with early forms of NS. MRI abnormalities observed in the frontal lobes, parietal lobes, and/or the temporoparietal junction suggest the presence of potential neural structural and network priority lesions associated with these deficits. Further research is necessary to determine whether these attention deficits can be ameliorated following anti-syphilis treatment and to investigate the mechanisms underlying specific neuronal damage caused by *T. pallidum* in vitro.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s40001-024-02004-1.

Additional file 1: Table 1. Demographic variables and attentional network test performance among NS, non-NS, and healthy controls.

Additional file 2: Figure 1. The diagram of attention network test.

Additional file 3: Figure 2. Patient 1, male, 50 years old, he was diagnosed with asymptomatic neurosyphilis due to persistent non-negative peripheral blood syphilis indicators after standard anti-syphilis treatment, Brain MRI showed multiple white matter hyperintensity in the frontal and temporal lobes..

Additional file 4: Figure 3. Patient 2, female, 67 years old, she was diagnosed with cerebral infarction due to recent walking instability, which was considered to be caused by vasculitis. Brain MRI showed bilateral frontal lobe, parietal lobe, and periventricular hyperintensity lesions.

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Author contributions
He Caifeng and Yuan Tao: study concept and design, definition of intellectual content, literature search, clinical studies, data acquisition, data analysis, statistical analysis, manuscript preparation, manuscript editing. Lu Xiaohong, Qiang Di and Wang Jun: clinical studies, data acquisition, data analysis Hu Wenlong and Yuan Lili: interpreted the data, statistical analysis. Cui Yong: definition of intellectual content, manuscript review. Shang Xianjin and Ci Chao: definition of intellectual content, data analysis, statistical analysis, manuscript preparation, manuscript editing and manuscript review.

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Data availability
The data supporting the conclusions of this article are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate
This study was approved by the Local Ethics Committee of Yijishan Hospital of Wannan Medical College. Written informed consent was obtained from all participants.

Competing interests
The authors declare no competing interests.

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References
1. Ropper AH. Neurosyphilis. N Engl J Med. 2019;381(14):1358–63.
2. Janier M, Unemo M, Dupin N, et al. 2020 European guideline on the management of syphilis. J Eur Acad Dermatol Venereol. 2021;35(3):574–88.
3. Chow F. Neurosyphilis. Continuum (Minneap Minn). 2021;27(4):1018–39.
4. Cai SN, Long J, Chen C, et al. Incidence of asymptomatic neurosyphilis in serofast Chinese syphilis patients. Sci Rep. 2017;7(1):15456.
5. Lee KW, Hong YJ, Lee SB, et al. Neurosyphilis as a rare cause of mild cognitive impairment and depression: two case reports and literature review. Dement Neurocogn Disord. 2021;20(4):112–5.
6. Gao JH, Ding DY, Qi YY, et al. Neuropsychological features in patients with general paresis of the insane at an early stage. Med Sci Monitor. 2022;28: e938316.
7. Mukherjee S, Srinivasan N. Attention in preferential choice. Prog Brain Res. 2013;202:117–34.
8. Posner MI, Petersen SE. The attention system of the human brain. Annu Rev Neurosci. 1990;13:25–42.
9. Petersen SE, Posner MI. The attention system of the human brain: 20 years after. Annu Rev Neurosci. 2012;35:73–89.
10. Fan J, McCandliss BD, Sommer T, et al. Testing the efficiency and independence of attentional networks. J Cogn Neurosci. 2002;14(3):340–7.
11. McDonough IM, Wood MM, Miller WS Jr. A review on the trajectory of attentional mechanisms in aging and the Alzheimer's disease continuum through the attention network test. Yale J Biol Med. 2019;92(1):37–51.
12. Lundervold AJ, Adolfsdottir S, Halleland H, et al. Attention Network Test in adults with ADHD–the impact of affective fluctuations. Behav Brain Funct. 2011;7:27.
13. Backes V, Kellermann T, Voss B, et al. Neural correlates of the attention network test in schizophrenia. Eur Arch Psychiatry Clin Neurosci. 2011;261(Suppl 2):S155-160.
14. Xiang L, Zhang T, Zhang B, et al. The associations of increased cerebral small vessel disease with cognitive impairment in neurosyphilis presenting with ischemic stroke. Brain Behav. 2021;11(6): e02187.
15. Gao JH, Li WR, Xu DM, et al. Clinical manifestations, fluid changes and neuroimaging alterations in patients with general paresis of the insane. Neuropsychiatr Dis Treat. 2021;17:69–78.
16. Yanhua W, Haishan S, Le H, et al. Clinical and neuropsychological characteristics of general paresis misdiagnosed as primary psychiatric disease. BMC Psychiatry. 2016;16:230.
17. Chen B, Shi H, Hou L, et al. Medial temporal lobe atrophy as a predictor of poor cognitive outcomes in general paresis. Early Interv Psychiatry. 2019;13(1):30–8.
18. Shang XJ, He CF, Tang B, et al. Neuroimaging features, follow-up analyses, and comparisons between asymptomatic and symptomatic neurosyphilis. Dermatol Ther. 2020;10(2):273–83.
19. He C, Kong Q, Shang X, et al. Clinical, laboratory and brain Magnetic Resonance Imaging (MRI) characteristics of asymptomatic and symptomatic HIV-negative neurosyphilis patients. J Infect Chemother. 2021;27(11):1596–601.
20. National Center for STD Control of Chinese Center for Disease Control and Prevention; Venereology Group of Chinese Society of Dermatology; Subcommittee on Venereology of China Dermatologist Association. Guidelines for diagnosis and treatment of syphilis, gonorrhea and genital Chlamydia trachomatis infection. Chin J Dermatol. 2020;53(03):168–79.
21. McCollum L, Karlawish J. Cognitive impairment evaluation and management. Med Clin North Am. 2020;104(5):807–25.
22. Lee SH, Yang H, Kang NR, et al. Re-emerging neurosyphilis in Korea as a possible etiology of psychotic disorders with pleomorphic symptoms and cognitive dysfunction: a case report and literature review. J Korean Med Sci. 2020;35(33): e271.
23. Li N, Li C, Xie X, et al. Impairment of attention network function in posterior circulation ischemia-evidence from the Attention Network Test. Front Hum Neurosci. 2022;16:1001500.
24. Cromarty RA, Schumacher J, Graziadio S, et al. Structural brain correlates of attention dysfunction in Lewy body dementias and Alzheimer's disease. Front Aging Neurosci. 2018;10:347.
25. Wang YQ, Pan Y, Zhu S, et al. Selective impairments of alerting and executive control in HIV-infected patients: evidence from attention network test. Behav Brain Funct. 2017;13(1):11.
26. Williams RS, Biel AL, Wegier P, et al. Age differences in the Attention Network Test: evidence from behavior and event-related potentials. Brain Cogn. 2016;102:65–79.
27. He C, Shang X, Liu W, et al. Combination of the neutrophil to lymphocyte ratio and serum toluidine red unheated serum test titer as a predictor of neurosyphilis in HIV-negative patients. Exp Ther Med. 2021;21(3):185.
28. Im JJ, Jeong H, Kim YD, et al. Regional cerebral blood flow abnormalities in neurosyphilis: a pilot SPECT study. Front Neurol. 2021;12: 726006.

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