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ORIGINAL ARTICLE

One for all, all for one: neuro-HIV multidisciplinary platform for the assessment and management of neurocognitive complaints in people living with HIV

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Abstract

Background: With ageing, comorbidities such as neurocognitive impairment increase among people living with HIV (PLWH). However, addressing its multifactorial nature is time-consuming and logistically demanding. We developed a neuro-HIV clinic able to assess these complaints in 8 h using a multidisciplinary approach.

Methods: People living with HIV with neurocognitive complaints were referred from outpatient clinics to Lausanne University Hospital. Over 8 h participants underwent formal infectious disease, neurological, neuropsychological and psychiatric evaluations, with opt-out magnetic resonance imaging

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(MRI) and lumbar puncture. A multidisciplinary panel discussion was performed afterwards, with a final report weighing all findings being produced.

Results: Between 2011 and 2019, a total of 185 PLWH (median age 54 years) were evaluated. Of these, 37 (27%) had HIV-associated neurocognitive impairment, but they were mainly asymptomatic (24/37, 64.9%). Most participants had non-HIV-associated neurocognitive impairment (NHNCI), and depression was prevalent across all participants (102/185, 79.5%). Executive function was the principal neurocognitive domain affected among both groups (75.5% and 83.8% of participants impaired, respectively). Polyneuropathy was found in 29 (15.7%) participants. Abnormalities in MRI were found in 45/167 participants (26.9%), being more common among NHNCI (35, 77.8%), and HIV-1 RNA viral escape was detected in 16/142 participants (11.2%). Plasma HIV-RNA was detectable in 18.4% out of 185 participants.

Conclusions: Cognitive complaints remain an important problem among PLWH. Individual assessment from a general practitioner or HIV specialist is not enough. Our observations show the many layers of HIV management and suggest that a multidisciplinary approach could be helpful in determining non-HIV causes of NCI. A 1-day evaluation system is beneficial for both participants and referring physicians.

KEYWORDS

ageing, HIV, multidisciplinary management of HIV, neurocognitive impairment, neuro-HIV

INTRODUCTION

In Switzerland, most people living with HIV (PLWH) have access to modern antiretroviral therapy (ART) [1], which is well tolerated and of low toxicity, enabling long-term viral suppression [1] and greater life expectancy [2]. However, with increased ageing, comorbidities such as neurocognitive impairment (NCI) also increase [3, 4]. Over the course of the HIV epidemic, NCI has shifted from severe and limiting HIV-associated dementia, present in up to 15% of PLWH during the pre-ART era [5], to milder clinical entities post-ART [6, 7].

Among participants of the Neurocognitive Assessment in the Metabolic and Ageing Cohort (NAMACO) study in Switzerland, between 27% and 40% of PLWH have been diagnosed with NCI [4, 8], based on the Frascati criteria, the 2007 consensus criteria for the diagnosis of NCI among PLWH, which classify HIV-NCI as asymptomatic neurocognitive impairment (ANI), mild neurocognitive disorder (MND), HIV-associated dementia (HAD), and non-HIV-associated neurocognitive impairment (NHNCI) [9]. Even if most NCI diagnoses are mild forms, the differential diagnosis and treatment of cognitive deficits is complex, in particular when different aspects (social, medical, pharmaceutical, stigma and psychological) of being a PLWH collide. The European AIDS Clinical Society (EACS) guidelines recommend a stepwise approach for the diagnosis and management of cognitive impairment in PLWH without obvious confounding conditions. In practice, such an approach requires weeks or months before all medical appointments are completed (neuropsychological assessment, neurological and cerebral spinal fluid examination, brain imaging, and infectious diseases evaluation) [10, 11]. Furthermore, there is a current lack of recommendations on when to address neurocognitive complaints or impairments in PLWH, especially when psychosocial factors intercept.

To best address this complexity, collaboration between HIV physicians and other disciplines is thus crucial. However, if formal communication is required between teams, this may delay diagnoses and/or therapeutic interventions. Moreover, serial referral to new medical departments can cause PLWH to become anxious about disclosure of their HIV status and HIV-related information, creating a barrier for achieving multidisciplinary care [12].

In 2011, as a response to these issues, we formalized and implemented a multidisciplinary Neuro-HIV consultation created for PLWH with cognitive and/or neurological complaints or impairment. To reduce the time required to see multiple specialists, we put in place a one-stop consultation spanning 8 h (one working day).

Here, we aim to incentivize fellow HIV clinics to consider this approach through a description of our functioning, findings, and experiences.

MATERIALS AND METHODS

Clinical setting

Lausanne University Hospital (CHUV) is a 1000-bed tertiary university hospital in Switzerland. It serves as a primary-level community hospital for around 300 000 inhabitants, and as referral hospital for 1–1.5 million inhabitants from southwest Switzerland. As part of the Infectious Diseases Service at CHUV, the Infectious Diseases Outpatient Service (IDOS) receives approximately 1500 people per year, of whom around 1200 are PLWH [13].

In a multidisciplinary approach for HIV care, the IDOS developed, in close collaboration with the Service of Neurology, the neuro-HIV platform in 2011, with the aim of evaluating and supporting PLWH with chronic neurological or cognitive complaints, namely memory issues, concentration difficulties or decision-making problems. PLWH are referred by infectious diseases specialists mainly, but not exclusively, from the French-speaking cantons of Switzerland (~ 2.5 million inhabitants). After formal request, each case is analysed in order to prioritize management (i.e. patients with long-standing complaints that were already addressed without success, such as initiation of antidepressants without improvement of symptoms). Referral times vary between three weeks and three months.

The PLWH attending the neuro-HIV platform are evaluated by: (i) an infectious diseases specialist, (ii) a neurologist, (iii) a neuropsychologist, and (iv) a psychiatrist. The participants are also offered brain magnetic resonance imaging (MRI), blood tests (routine, and specific serologies or biomarkers of interest) and lumbar puncture (LP). All tests and assessments are performed during an 8 h period (8:00 AM to 4:00 PM) **(**Figure 1**)**. Regarding neurocognitive impairment, all interventions are framed within the EACS recommendations [10, 11, 14], where PLWH with suspected neurocognitive problems or with neurocognitive complaints should undergo a neuropsychological (NP) assessment in case these problems persist after an initial assessment (i.e. using a screening questionnaire [15]), and depression and anxiety are excluded or optimally managed. After an initial evaluation, participants may be offered follow-up consultations if required. Management of participants is discussed during a multidisciplinary meeting with all the specialists at the end of the day. A final report is issued, signed by every specialist, containing a summary of all consultations, complementary tests and proposed therapeutic interventions. The neuro-HIV platform takes place once a month, on average, with one to three participants consulted at a time.

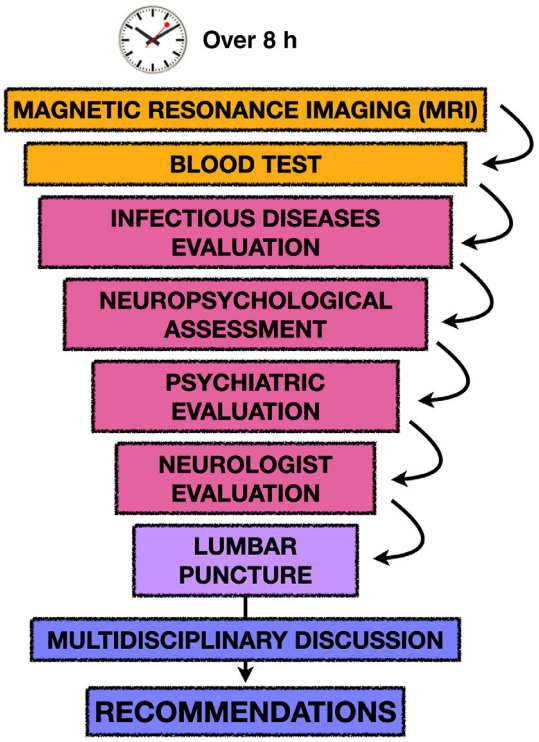

FIGURE 1 Assessments performed in our neuro-HIV clinic. Evaluations do not follow a specific order with the exception that MRIs are performed before lumbar puncture to ensure that this procedure does not represent a risk for the patient

Infectious diseases evaluation

This evaluation consists of a full medical history and clinical examination. During the consultation, topics such as HIV natural history, understanding of HIV disease, current antiretroviral treatment, adherence to treatment (facilitators and barriers), HIV-genotype resistance analysis and comorbidities are discussed with the participants. On blood analysis, HIV viral loads < 20 copies/mL are considered undetectable. If an LP is performed, central nervous system (CNS) HIV-RNA viral escape is defined as: (i) the presence of quantifiable HIV-RNA in the cerebrospinal fluid (CSF) at any level with undetectable plasma HIV-RNA, or (ii) CSF HIV-RNA greater than plasma HIV-RNA when the latter is detectable [16].

Neurological evaluation

Participants also undergo neurological evaluation and clinical examination, mainly to rule out potential neurological

differential diagnoses (e.g. extrapyramidal signs) for cognitive decline. In addition, all participants are offered brain MRI and LP, as opt-out universal testing. Since 2013, therapeutic levels of ART agents in the CSF have been measured through liquid chromatography and mass spectrometry [17, 18].

MRI

Participants underwent a 3 T MRI protocol encompassing a high-resolution, T1-weighted magnetization-prepared rapid gradient echo (MPRAGE) acquisition for anatomical reference; an MP2RAGE acquisition with the same voxel and matrix size to obtain T1 relaxation maps [19]; and a multiple echo Fast Low Angle SHot (FLASH) with and without magnetization transfer preparation. The signals acquired with (MT) and without (M0) magnetization saturation pulse were used to compute magnetization transfer ratio (MTR) maps as reported previously [20]. Moreover, T2 star maps were calculated using a monoexponential fitting [20]. Brain segmentation into grey and white matter (GM and WM, respectively) was performed using Morphobox and Freesurfer [21].

Neuropsychological assessment

Participants complete a NP assessment covering the specific cognitive domains relevant for HIV-associated NCI [9, 22] and tailored to each patient. We particularly evaluate instrumental functions (oral and written language, praxis and gnosis), memory (autobiographical, episodic and short-term), executive function and attention. We avoid employing a 'fixed' NP test battery, and select the test best reflecting patient's complaints, but also the most appropriate in terms of norms and challenges for their age and level of education. This allows for a more refined and precise description of each patient's cognitive function [23].

Trained neuropsychologists perform the NP assessment, lasting up to 90 minutes. Raw scores derived from individual neurocognitive tests are converted to demographically adjusted standard scores (z-scores). Participants are then classified, based on their z-scores according to the Frascati criteria, into ANI, MND, HAD or NHNCI [9] (Figure A1).

In addition to NP testing, functional impairment is assessed using Lawton's Instrumental Activities of Daily Living (IADL), and Patient's Assessment of Own Functioning Inventory questionnaire (PAOFI) where impairment is defined as difficulties in at least two items out of 11 (Figure A1). Cognitive complaints are also assessed using three screening questions asking participants if they experience problems with memory, concentration and mental slowing when reasoning, as previously described [4, 8, 15]. For each of the three screening questions, response options are: 'never', 'hardly ever' or 'yes, definitely' [15].

Psychiatric evaluation

This assessment, which takes up to 1 h, focuses on household, social and professional context, as well as psychiatric personal and family history. Depressive symptoms are assessed using the Montgomery–Åsberg Depression Rating Scale (MADRS), where scores between 12 and 19 are considered to demonstrate a risk of mild depression, scores of 20–34 represent moderate depression, and scores >34 represent severe depression. This evaluation helps to estimate the extent to which cognitive problems could be attributed to psychopathology and/or the need for psychiatric follow-up.

Ethical considerations

The ethics committee of the Canton of Vaud approved the neuro-HIV platform protocol in 2011 (study protocol number 44/11). All participants signed specific informed consent.

RESULTS

Between March 2011 and April 2019, the neuro-HIV platform assessed 185 PLWH. Participants were of median age 54 years [interquartile range (IQR): 47–61], were predominantly male (58.9%), white (72.9%), men who have sex with men (MSM; 24.8%), single (40.5%) and employed (50.5%). A total of 76 (41.1%) women participated, 32 (42.1%) of whom were of African origin. Participants' clinical characteristics are presented in Table 1.

Based on the Frascati criteria, we found that 37 participants (20%) had HIV-associated NCI, with 24 (12.9%) diagnosed with ANI, 11 (5.9%) with MND, and 2 (1.1%) with HAD. On the other hand, 102 participants (55.1%) had NHNCI **(**Figure 2**)**. The median global z-score for PLWH with NHNCI was −0.44 (IQR: −1.1–0.06). The majority of participants with NHNCI had depression (80, 79.5%) based on MADRS score and psychiatric evaluation overall; other causes of NHNCI were diverse: progressive multifocal leukoencephalopathy (PML), drug and alcohol abuse, learning disabilities, toxoplasmosis or other infectious diseases sequelae, or undetermined. There were no differences between female and male

TABLE 1 Neuro-HIV platform patient characteristics

HIV clinical parameters	*n* (%)
Time since HIV diagnosis (years, IQR)	13 (7.5–21)
CD4 nadir (cells/μL, IQR), missing = 11	185.5 (66–294)
Current CD4 count (cells/μL, IQR)	591 (405.5–763)
Serum VL > 20 (copies/mL)	34 (18.4)
CNS HIV viral escape	16 (11.2)
AIDS, missing = 1	103 (58.2)
Currently on antiretroviral therapy	180 (97.3)
Currently on efavirenz	21 (11.4)
Hepatitis C	22 (14.9)
Syphilis	26 (17.1)
Cardiovascular risk factors	
Smoke	74 (40.0)
Cardiovascular disease	31 (16.8)
Metabolic disease	15 (8.1)
Hyperlipidaemia	38 (20.5)
Obesity	27 (14.6)
Depression	42 (22.7)

Abbreviations: CNS, central nervous system; IQR, interquartile range; VL, viral load.

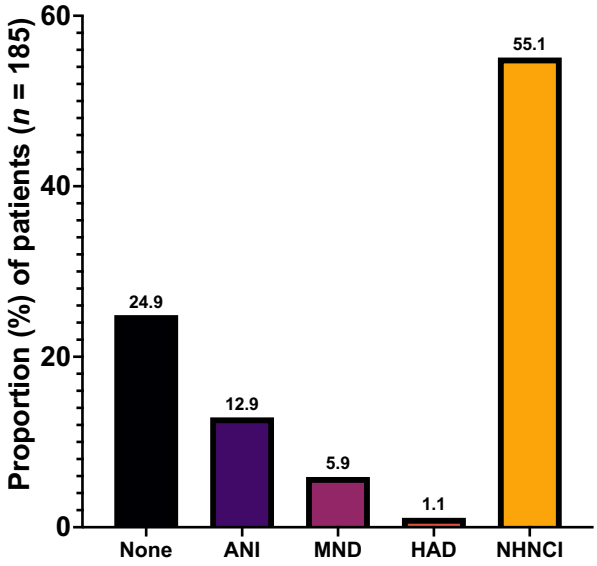

FIGURE 2 Neurocognitive diagnoses among patients assessed in the neuro-HIV platform (according to the Frascati criteria). Numbers are percentages (%). ANI, asymptomatic neurocognitive impairment; HAD, HIV-associated neurocognitive impairment; MND, mild neurocognitive disorder

PLWH regarding neurocognitive impairment (72.5% vs 78.9%, $p = 0.4$). Among participants of African origin (37, 20%), a total of 34 (91.9%) had NCI, 24 of whom (70.5%) had NHNCI. However, this difference was not statistically significant ($p = 0.2$). There were no differences between the proportion of cognitive diagnoses by age group ($p = 0.3$) and by time since HIV diagnosis ($p = 0.2$).

Neurological findings were equally prevalent among participants with HIV-associated NCI and NHCNI (21.6% vs 21.5%). The most common neurological manifestation was polyneuropathy in 29 participants (15.7%), followed by radicular pain in eight (4.3%) participants. Notably, a total of four participants (2.16%) had PML, all of them with a NHNCI diagnosis.

In all, 143 participants (77.3%) underwent LP. In the other participants, the LP was either declined or not feasible. Out of the 143 participants who underwent LP, 16 (11.2%) had HIV viral escape of whom the majority (11, 69%) had an initial diagnosis of NHNCI. Median HIV-1 RNA in CSF was 49 copies/mL (IQR: 35–190). We could not identify any difference in terms of symptoms, complaints, or psychiatric or neuropsychological assessment that differentiated cognitive impairment with or without HIV-1 CSF viral escape.

A total of 167 participants (90.3%) underwent brain MRI, with 45 (26.9%) having abnormal results. Of those, 35 (77.8%) were diagnosed with NHNCI, six (13.3%) with HIV-associated NCI (five with ANI and one with MND), and four (8.9%) were unimpaired. Abnormal MRI findings were more prevalent among participants with NHNCI [35 (85.4) vs 6 (14.6) with HIV-associated neurocognitive disorder, $p = 0.03$]. In general, 35 (20.9%) MRIs reported cortical atrophy, 26 (15.5%) subcortical atrophy, five (3.0%) gadolinium-enhanced lesions, and one (0.6%) a lesion and mass effect, with overlapping of these findings among participants (Figure 3).

Recommendations for participants' management are presented in Table 2. Of the 185 patients evaluated for the first time, 69 (37.3%) were offered follow-up evaluations at the neuro-HIV platform, of whom 21 (30.4%) re-attended. Out of these 21 patients, cognitive function improved in two participants (9.5%), deteriorated in one (4.8%; developed ANI when previously no NCI), and remained unchanged in 14 participants (66.7%). Four PWLH (19%) developed NHNCI at follow-up.

As the large majority of participants were referred to the neuro-HIV platform by HIV physicians, follow-up by an HIV specialist was recommended only in a small number of cases (see Table 2**)**. Main treatment recommendations after psychiatric evaluation were initiation or modification of antidepressive treatment in 63 participants (34.1%), while neurological recommendations were mainly related to management of comorbidities such as epilepsy or progressive multifocal leukoencephalopathy.

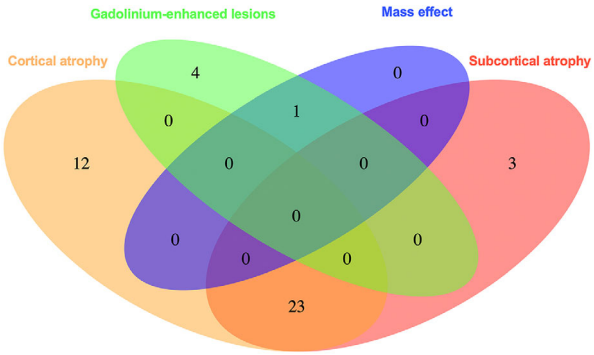

FIGURE 3 Frequency of magnetic resonance imaging (MRI) findings across patients with abnormal MRI results ($n = 45$). Each colour represents a different group of findings at the MRI. Overlapping of colours represents multiple findings in the same patient

TABLE 2 Management and suggestions after the multidisciplinary single-day clinic

Infectious diseases	*n* (%)
ART change/simplification	60 (32.4)
Follow-up with an HIV specialist	20 (10.8)
Follow-up/increase adherence[a]	24 (12.9)
Neurology	
Follow-up neurological consultation	28 (15.1)
Initiation of neurological treatment	19 (10.3)
Neuropsychology	
Follow-up of neurocognitive tests	69 (37.5)
Psychiatry	
Change/initiation of psychiatric medication	63 (34.1)
Psychiatric and psychotherapeutic follow-up	83 (45.4)
Control of comorbidities	50 (27.1)

Abbreviation: ART, antiretroviral therapy.
[a]Follow-up of adherence was performed using electronic pill monitoring, pill reminders and, in rare cases, measurement of drug levels.

DISCUSSION

People living with HIV attending the neuro-HIV platform between 2011 and 2019 varied widely in age (22–79 years) and in time since HIV diagnosis (1–34 years). Participants were predominantly male, white and MSM, reflecting the overall demography of PLWH in Switzerland [1]. Plasma HIV-RNA was detectable in 18.4% of participants. All but two participants were on ART at the time of assessment.

After classifying NCI based on the Frascati criteria [9], we found differences in the proportion of participants with a diagnosis of HIV-associated and non-HIV-associated NCI. Overall, NCI has been reported among up to 40% of PLWH in the post-ART era in Western countries [4, 24, 25]. In Switzerland, the majority of data regarding NCI among PLWH comes from the Neurocognitive Assessment in the Metabolic and Aging Cohort (NAMACO) study, which is nested within the Swiss HIV Cohort Study (SHCS) [1]. Baseline NAMACO study data from 981 PLWH demonstrated an overall NCI prevalence of 40% [4]. Among PLWH referred to the neuro-HIV platform for neurological and cognitive complaints, 75% had NCI, with NHNCI representing 73.4% of the whole NCI group (55.1% of all platform participants had NHNCI). This NHNCI prevalence is around four times higher than that among participants of the NAMACO study, where NHNCI prevalence was 13% at baseline and 10% at 2-year follow-up [4, 8]. We also found NHNCI to be particularly prevalent among female participants, who were mainly of African origin, where NHNCI was more prevalent than among male participants of the same origin. Although these differences are difficult to interpret, we observed a larger affection among this group on working and episodic memory, domains that have been previously identified to be more affected among female than male PLWH [26, 27].

Globally, we attribute the differences in NHNCI prevalence between neuro-HIV platform participants and NAMACO study participants to different factors: (i) referral bias (probably the most determinant factor), as participants are referred to the neuro-HIV platform with either cognitive and/or neurological complaints, or after an objective evaluation from general practitioners or HIV specialists, whereas the NAMACO study enrols PLWH aged ≥ 45 years who can be asymptomatic or symptomatic; (ii) neuro-HIV platform participants undergo formal evaluation by a psychiatrist rather than assessment by screening tools [i.e. the Centre for Epidemiological Studies Depression Scale (CES-D) score used in the NAMACO]; and (iii) multidisciplinary evaluation and discussion of participants enable a review of all factors potentially affecting NCI and may highlight non-HIV-associated factors otherwise missed. In short, the neurocognitive and neuropsychiatric evaluation, being customised in the platform as opposed to standardized in NAMACO, offers more precise diagnoses.

Prevalence of ANI among platform participants was lower than in previous reports from the NAMACO study as well as other multicentre studies [4, 24, 25]. This is expected, given that participants were referred to the platform based on cognitive complaints or pathological cognitive screening tests. Notably, the clinical significance of ANI remains controversial since, by definition, this entity does not have an impact on everyday life [8, 28]. Thus, we need to ask whether ANI is not simply a variation of the norm, especially considering that many works studying ANI do not entail a control HIV-negative matched group.

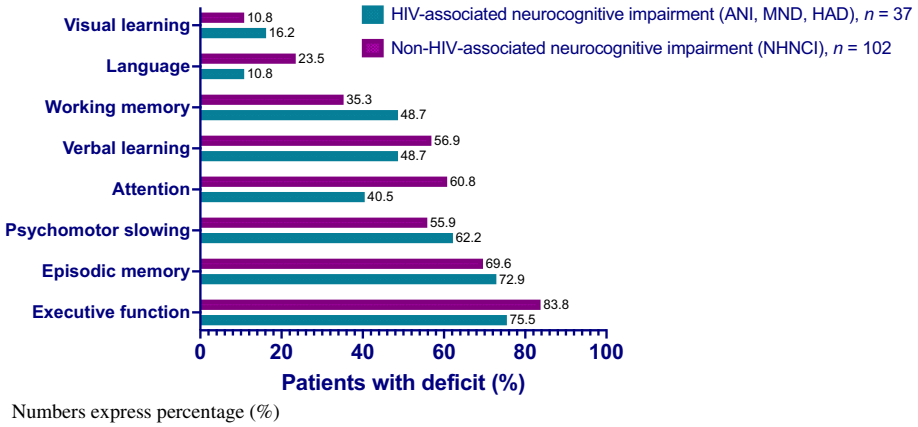

FIGURE 4 Neurocognitive impairment by cognitive domain among patients evaluated in the neuro-HIV platform. Numbers are percentages (%)

After an extensive search, we have only identified one HIV clinic in the UK (referred to as the 'orange clinic') which evaluates PLWH in a comparable way (referrals from outpatient clinics, participants with neurocognitive complaints, multidisciplinary approach, including a psychiatric evaluation). This group also found a larger prevalence of NHNCI than most studies (27%) [12]. Although this proportion is lower than ours, it is striking that in both centres with a multidisciplinary team, NHNCI is more prevalent than HIV-associated NCI [4, 24]. The other striking feature is that our neuro-HIV platform and the 'orange clinic' provide a similar service, despite functioning within markedly different healthcare systems – insurance-based healthcare in Switzerland and a free-at-the-point-of-care National Health Service in the UK – suggesting that the multidisciplinary model is feasible in different settings.

One important factor identified in our participants, and closely related to NHNCI, was depression. Depression is twice as frequent among PLWH compared with the general population and its prevalence does not decline with age, contrary to the HIV-negative population [29, 30]. High depression rates among PLWH could be due to a negative reaction to HIV diagnosis and/or an organic cause, such as CSF viral escape, persistent inflammation (e.g. due to ART, cardiovascular disease or opportunistic infections), or something else [31, 32]. As was the case for other researchers [33], we found that the cognitive domains affected by depression were motor skills, executive function, attention, working memory functions and verbal episodic memory **(**Figure 4**)**. Moreover, PLWH with depression usually present cognitive complaints [14]. Management of depression includes antidepressant medication and psychiatric or psychotherapeutic interventions. Almost half of our participants were advised to start, continue or modify their antidepressant medication, and almost a third to consider starting or continuing psychiatric or psychotherapeutic follow-up. Recently, these interventions, when supported by cognitive behavioural components, have shown to be effective in management of depression among PLWH [34–36]. We believe that the large prevalence of depression in PLWH, the need for adequate therapy, and the importance of distinguishing between organic and non-organic neurocognitive symptoms among PLWH highlight the importance of the role of the psychiatrist in evaluating PLWH with NCI or neurocognitive complaints.

Regarding imaging, we found both cortical and subcortical anomalies mainly among participants diagnosed with ANI or NHNCI, with no structural anomalies among those with MND or HAD. Usually cortical abnormalities are described in PLWH with ANI, while those with MND and HAD display more global (cortical and subcortical) abnormalities [37]. Although some studies have found structural alterations among PLWH with depression [38], the large prevalence of MRI alterations among PLWH with NHNCI could be a consequence of a 'legacy' effect, or due to previous opportunistic infections with an impact in the CNS. In our platform, MRI findings were not specific, did not correlate with cognitive symptoms and/or complaints, and usually did not have a substantial impact on our clinical reasoning and management. In summary, the primary role of MRI was to exclude other pathology rather than to identify radiological features of HIV-associated NCI.

Another intervention proposed in the neuro-HIV platform was ART modification. ART change was suggested in participants who had CSF HIV viral escape. Detailed information regarding CSF HIV viral escape withing the neuro-HIV platform is part of another publication by Filippidis et al., currently under review. Recommendations were also made when simplified treatment regimens could be more convenient and/or could HIV treatment adherence.

Adherence surveillance was recommended in around 12% of participants, mostly in the context of virological failure, and/or initiation of new regimens. Different methods for adherence surveillance were proposed, from directly observed therapy to monitoring via medication event monitoring systems (MEMS). MEMS have been shown to decrease gaps in treatment and decrease treatment failure [39]. A previous study from our group, which included PLWH assessed in the neuro-HIV platform, showed a decline in neurocognitive performance among participants with low (<50%) ART adherence [40]. These strategies were recommended in tandem with assessment and interventions related to the participants' environment, particularly for individuals coming from underserved settings with psychological and/or social challenges.

Regarding comorbidity management, it was related mainly to pharmacological management of cardiovascular disease and advice on lifestyle. We highlight this intervention, as cardiovascular risk factors have been previously associated with neurocognitive impairment among PLWH [41, 42]. A recent study following PLWH for over 12 years found that comorbidities, including cardiovascular diseases, were associated with neurocognitive decline regardless of age, HIV disease or ART characteristics [43]. Among our participants, 69% of PLWH with any cardiovascular risk (119 participants) had NHNCI. Besides therapeutic interventions, social counselling and support were recommended for participants where non-HIV external factors such as financial difficulties, concerns related to migration status, unemployment, lack of health insurance and loss of relatives could be exacerbating cognitive symptoms.

Conversely, none of the 185 PWLH assessed at the neuro-HIV platform received specific cognitive neurorehabilitation. Indeed, pharmacological options to preserve cognitive function or promote cognitive recovery in PWLH are very limited, if they even exist. Therefore, there is a crucial need for efficient multidisciplinary neurorehabilitation in neuro-HIV (mainly neuropsychology and occupational therapy) [44, 45]. Computerized cognitive neurorehabilitation has yielded some promising effects [46] and may represent a rather accessible approach in the near future.

Our report has limitations. First, our demographics (predominantly male, white and MSM) limit the generalizability of our findings. Moreover, although follow-up of all participants was not a goal of the platform, and re-evaluations were not requested by physicians in most cases, we do not know if recommended interventions were successful or even implemented. We also are unaware if participants with MND or ANI developed more severe NCI. Furthermore, regardless of the knowledge that several non-medical interventions were recommended (psychosocial support, legal advice, seek of economic aid) we did not quantify them, limiting our expertise to the intersection of social and biological factors of HIV and NCI. Nevertheless, comforting to us, in another report, we have assessed satisfaction related to the neuro-HIV platform, and found that three-quarters of participants and referring doctors considered the platform useful or essential [47].

CONCLUSION

Cognitive complaints remain an important problem among PLWH, and in some cases an individual assessment from a general practitioner or HIV specialist is not enough. In this report, we have outlined a multidisciplinary approach to assessing and managing neurocognitive issues in PLWH. Although we focus on PLWH with neurocognitive symptoms, our observations demonstrate the many layers of current HIV management, where biomedicine, psychiatry and sociology intersect. In particular, our data suggest that multi-faceted evaluation involving a psychiatrist is helpful in determining non-HIV-related causes of NCI in PWLH, leading to different, specific management strategies. We conclude that a multidisciplinary approach could be beneficial in neuro-HIV management and believe that the model we describe, a one-day, one-stop platform, is beneficial to both PLWH and referring physicians.

AUTHOR CONTRIBUTIONS

PB, PF and BV contributed to data acquisition and created the original database. JD performed data curation, the formal statistical analysis, and wrote the original draft. IND, MB, LV, AS and VD contributed to data acquisition and interpretation. KEAD conceptualized the study and contributed to data interpretation and editing of the original draft. AB, GM, RDP, CG and MC conceptualized, implemented and supervised the neuro-HIV platform. All authors reviewed and approved the manuscript and agree to be accountable for all aspects of the work.

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CONFLICTS OF INTEREST

JD, IND, MB, LV, AS, AB, GM, PF, BV, CG, VD, RDP report no conflicts of interest related to this work. MC's

institution has received research grants from Gilead, MSD and ViiV unrelated to this publication and meeting fees from Gilead unrelated to this publication, and offered expert testimony for Gilead, MSD and ViiV. KEAD's institution has received research funding from Gilead unrelated to this publication and offered expert testimony for MSD.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ETHICS STATEMENT

The ethics committee of the Canton of Vaud approved the neuro-HIV platform protocol in 2011 (study protocol number 44/11). All participants signed specific informed consent. Data from this study are available upon reasonable request contacting correspondence author (JD) and/or principal investigators (RDP, MC). The neuro-HIV platform received funding from ViiV Healthcare and Gilead Sciences; however, funders: (i) did not have access to data and/or participants information, (ii) did not have a role in clinical and data assessment; (iii) did not request ad hoc or post hoc analyses; and (iv) did not have any role in the drafting of our manuscript.

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APPENDIX

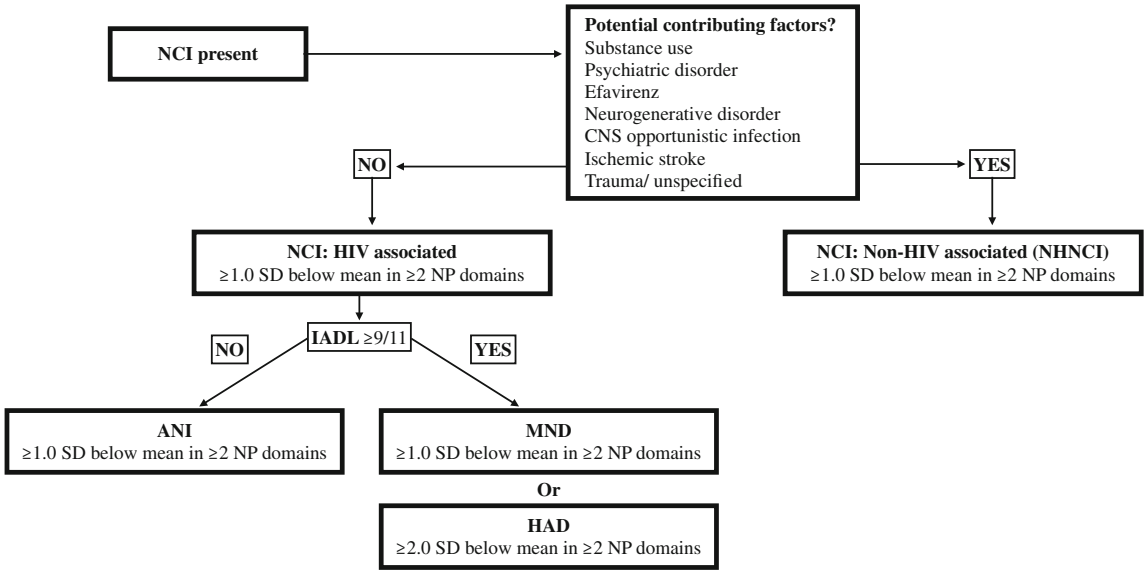

FIGURE A1 Neurocognitive assessment classification algorithm based on the Frascati criteria [9]. ANI, asymptomatic neurocognitive impairment; HAD, HIV-associated dementia; IADL, Instrumental Activities of Daily Living; MND, mild neurocognitive disorder; NCI, neurocognitive impairment; NHNCI, non-HIV-associated neurocognitive impairment; NP, neuropsychological; SD, standard deviation.