Low levels of activated and senescent T cells characterize persons with HIV-1-associated neurocognitive disorders

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Summary

Neurocognitive impairment (NCI) may be observed in up to 60% of people living with HIV (PLWH) on efficient antiretroviral therapy. After adjusting on age, sex, education, comorbidities and social confounding factors, we have recently observed a 74% increased risk of HIV-associated neurocognitive disorder (HAND) in ageing PLWH.

In order to better define the type of immune activation linked to NCI in PLWH, we used supervised and non-supervised global approaches looking among 31 peripheral immune activation markers for biomarkers associated with clinical and imaging signs of NCI.

To our surprise, NCI was preferentially characterized by low levels of circulating activated T cell.

The double hierarchical clustering identified **six different immune activation profiles among participants**. Participants with one of these profiles, Profile 1, presented more frequently ANI and MND (odds ratio 8.8 [95% CI 1.0-77.0], p = 0.041) than the participants with other profiles.

These findings raise the interesting hypothesis that T cell recruitment into the CNS might play a pivotal role in NCI.

Low percentage of activated T cells in the blood of people living with HIV-1 and neurocognitive disorders : a consequence of their intracerebral recruitment ?

Further informations:

Method :

Study design:
This is an ancillary study of the ANRS EP58 HAND 55-70 project which evaluated the prevalence of NCI in PLWH on efficient cART (Clinical trial registration NCT02592174). Seventy-nine PLWH were sequentially recruited at the University Hospitals of Montpellier and Nîmes, France.

Cognitive and functional evaluations:
Volunteers went through a series of tests to be classified according to the Frascati classifications. They are classified in four groups: Neurocognitively unimpaired (UN); Asymptomatic (ANI); Mild neurocognitive disorder (MND) and HIV-associated Dementia (HAD). We did not have HAD in our cohort.

Flow cytometry:
Combinations of 18 monoclonal antibodies were used to label and characterise subpopulations of PBMCs for each volunteer.

Immunologic markers in peripheral blood:
Elisa was used to quantify soluble markers in plasma.

Magnetic resonance imaging:
Neuroimaging data were collected on a 3T MRI (MAGNETOM Skyra, Siemens Healthcare, Germany). The Fazekas scale was used to quantify the amount of white matter T2 hyperintense lesions between 0 to and 4. We split the patients in two groups: 0-1 or 2 and more.

Statistics:
Volunteers were classified per immuno-profile using a double hierarchical ascendant clustering, one at the participant level, and the other one at a marker level.
Groups were compared with Student Welch correction, as standard deviations were not equal.

Results :