# Effect of Non-HIV Drugs on Neurocognitive Domains in a Well-Treated HIV Population

**Bernadette Jakeman**[1,2], Alexandra Scherrer[3,4], Katharine E.A. Darling[5], Isaure Nadin[6,7], Barbara Hasse[3], Christoph Hauser[8], Philip Tarr[9], Alexandra Calmy[10], Ursula Kunze[11], Marcel Stoeckle[2], Patrick Schmid[12], Manuel Battegay[2], Renaud Du Pasquier[6], Matthias Cavassini[5]*, Catia Marzolini[2]* and the NAMACO study group a Swiss HIV Cohort Study

* co-shared last authors

[1]Department of Pharmaceutical Practice and Administrative Sciences, University of New Mexico College of Pharmacy, Albuquerque, USA; [2]Division of Infectious Diseases and Hospital Epidemiology, Departments of Medicine and Clinical Research, University Hospital Basel, University of Basel, Switzerland; [3] Division of Infectious Diseases and Hospital Epidemiology, University Hospital Zurich, Switzerland; [4]Institute of Medical Virology, University of Zurich, Switzerland; [5]Service of Infectious Diseases, University Hospital Lausanne, University of Lausanne, Switzerland; [6]Service of Neurology, Department of Neurosciences, University Hospital Lausanne, University of Lausanne, Switzerland; [7]Service of Neurology, University Hospital Geneva, Switzerland; [8]Department of Infectious Diseases, University Hospital Bern, University of Bern, Switzerland; [9]University Department of Medicine, Kantonsspital Bruderholz, University of Basel, Switzerland; [10]Division of Infectious Diseases, University Hospital Geneva, University of Geneva, Switzerland; [11]Memory Clinic, Felix Platter Hospital University Center for Medicine of Aging, Basel, Switzerland; [12]Department of Infectious Diseases and Hospital Epidemiology, Cantonal Hospital St Gallen, Switzerland

Contact
Bernadette Jakeman, PharmD
University of New Mexico
Email: Bjakeman@salud.unm.edu

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## Introduction

- Neurocognitive impairment (NCI) remains a problem in people living with HIV (PLWH) despite advances in HIV management.
- Exposure to medications with anticholinergic (ACH) activity has been associated with NCI in aging HIV-negative persons [1], in HIV-infected women [2] and was shown to contribute to self-reported NCI in PLWH ≥ 65 years old of the Swiss HIV Cohort Study (poster 410).
- Aim: to evaluate the effect of ACH and sedative medications on neurocognitive function in well-treated PLWH who underwent detailed neuropsychological (NP) evaluation.

## Methods

- Study population: participants enrolled in the prospective Neurocognitive Assessment in Metabolic and Aging Cohort (NAMACO) based on the following inclusion criteria: HIV-positive status; age ≥ 45 years and sufficient oral fluency to undergo a thorough NP evaluation. Participants were enrolled regardless of NCI symptoms between May 2013 and November 2016 [3].
- NP assessment: performed by trained neuropsychologists and covered 7 cognitive domains (table below). Binary outcomes (presence/absence of impairment) were assessed for each individual neurocognitive domain and were combined to determine the overall neurocognitive function.

| Neurocognitive domain | NP tests |
|---|---|
| Motor skills | Finger tapping, grooved pegboard |
| Speed of information processing | Wechsler adult intelligence scale, 4th ed (WAIS-IV), coding, colour trails 1 |
| Attention/working memory | WAIS-IV digit span |
| Executive function | Category fluency, 5-point figural fluency, victoria stroop, colour trails 2 |
| Verbal learning memory | Hopkins verbal learning test - revised |
| Language | Category fluency, victoria stoop |
| Sensory skill | Grooved pegboard, victoria stroop |

- Medication review: ACH medications were identified using a previously developed ACH scale (poster 410). ACH activity was scored 1 to 3, with a higher score indicating more ACH activity. Medications with known sedative properties (i.e. opioids, muscle relaxants, anticonvulsants, anxiolytics and sedatives) were also identified.
- Statistics: multivariable logistic regression models were used to explore the effect of drugs on overall neurocognitive function and on individual neuro-cognitive domains. Tested drug groups:
  - i) ACH drugs (ACH ≥ 1 = being on at least one ACH drug)
  - ii) high ACH score (total ACH score ≥ 3)
  - iii) sedative drugs (being on at least one drug with sedative properties)
  - iv) ACH + sedative drugs

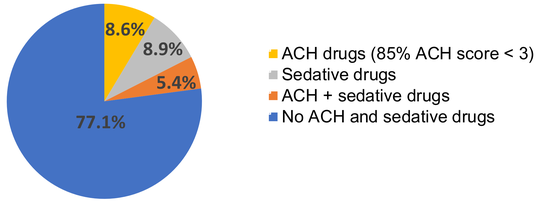
  Models were adjusted for demographics, HIV history, comorbidities, alcohol binge, illicit substance use, and efavirenz/dolutegravir use.

## Results

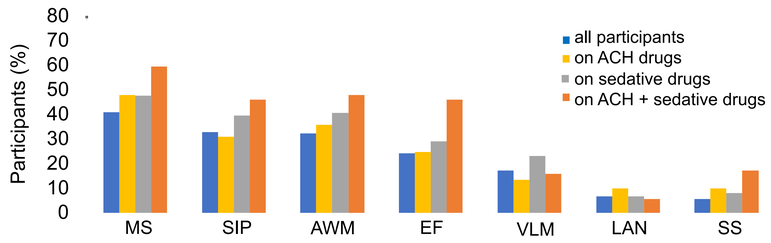
| Characteristics of Study Population | | N = 963 |
|---|---|---|
| Median age, years (IQR) | | 52 (49-59) |
| Male sex (%) | | 769 (79.9) |
| Caucasian origin (%) | | 883 (91.7) |
| Median education duration, years (IQR) | | 13 (12-14) |
| Mode HIV acquisition (%): | MSM | 497 (51.6) |
| | heterosexual | 320 (33.2) |
| | IDU | 115 (11.9) |
| Alcohol binge (monthly/weekly/daily)* (%) | | 61 (6.3) |
| Current use of cannabis/cocaine/heroine (%) | | 123 (12.8) |
| Cigarette smoking (%) | | 312 (32.4) |
| Diabetes (%) | | 60 (6.2) |
| Hypertension (%) | | 258 (26.8) |
| History of cardiovascular events (%) | | 38 (3.9) |
| History opportunistic infection of CNS (%) | | 43 (4.5) |
| Depression (%) | | 139 (14.4) |
| Hepatitis B co-infection (%) | | 452 (46.9) |
| Hepatitis C co-infection (%) | | 167 (17.3) |
| History of syphillis (%) | | 245 (25.4) |
| HIV viral load < 50 copies/mL (%) | | 924 (96.0) |
| Current median CD4 count (cells/uL) (IQR) | | 633 (468-815) |
| Median nadir CD4 count (cells/uL) (IQR) | | 180 (75-270) |
| On antiretroviral treatment (%) | | 950 (98.7) |
| On dolutegravir or efavirenz containing treatment (%) | | 286 (29.7) |
| Median antiretroviral treatment duration, years (IQR) | | 12 (6-17) |
| Median number of non HIV-drugs (IQR) | | 2 (1-4) |
| Polypharmacy (≥5 non-HIV drugs) (%) | | 117 (12.1) |

* alcohol binge on a monthly or weekly or daily basis

### Prevalence of ACH and sedative drugs use in participants



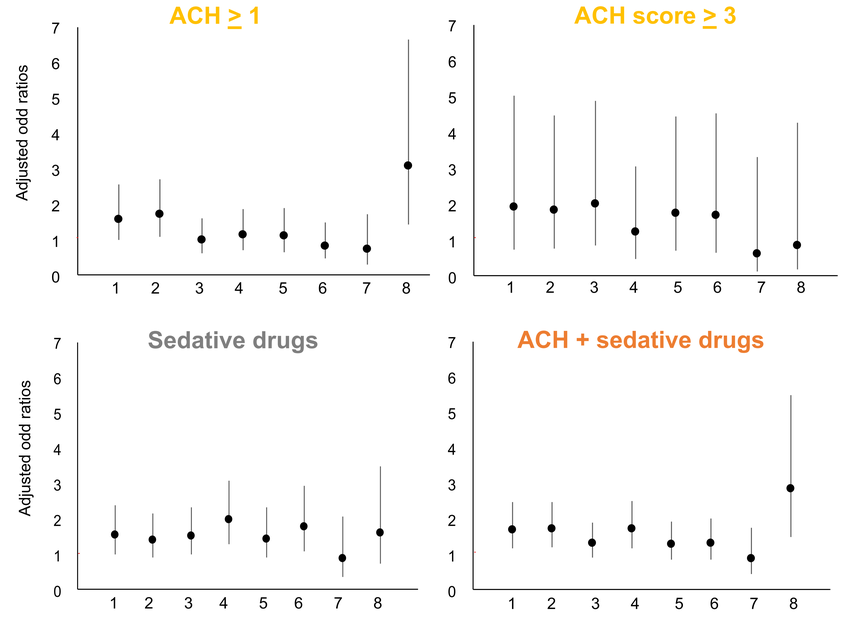

### Prevalence of participants with deficits in each individual domains




MS=motor skills; SIP=speed of information processing; AWM=attention/working memory; EF=executive function; VLM=verbal learning memory; LAN=language; SS=sensory skills

## Results

### Effect of ACH and sedative drugs on neurocognitive function




1: overall NC function 2: motor skills 3: speed of info. processing 4: attention/working memory
5: executive function 6: verbal learning memory 7: language 8: sensory skills

Multivariable logistic regression models adjusted for: age, gender, ethnicity, level of education, HIV transmission risk group, alcohol binge, current use of cannabis, cocaine or heroine, history of cardiovascular events, diabetes, hypertension, dyslipidemia, cigarette smoking, history of opportunistic infection of CNS, depression, hepatitis B and C co-infections, syphillis, CD4 cell count, duration of antiretroviral treatment, efavirenz or dolutegravir based treatment.

- ACH drugs were associated with impairment of motor and sensory skills domains and sedative drugs were associated with impairment of attention and verbal learning domains.
- Increased risk of overall NCI was associated with sedative drugs and was borderline for ACH drugs (OR, 95% CI: 1.58, 0.98-2.55). Other significant risk factors for overall NCI were older age, lower education and being non-Caucasian.

## Conclusion

- **Non-HIV drugs can contribute to NCI with ACH drugs impairing motor and sensory functions and sedative drugs altering the attention and learning functions. HIV clinicians need to consider these drugs when assessing NCI.**
- **Future studies should evaluate the impact of stopping/substituting ACH and sedative drugs on neurocognitive performance.**

### References

1) Fox C et al. J Am Geriatr Soc 2011; 2 ) Rubin L et al. JAIDS 2018; 3) Metral M et al. HIV Medicine 2020