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HIV and Neurocognitive Impairment: Scope of the Problem

- Gabriele Arendt
- Dept. of Neurology, University of Duesseldorf, Medical Faculty, Germany
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“Disclosures”



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HIV Associated Neurocognitive Disorders (HAND)

Primary HAND

- Asymptomatic neurocognitive impairment
- Mild neurocognitive disorder
- HIV-associated dementia

Secondary HAND

- Infection
- Neoplasia
- Cerebrovascular
- Nutritional
- Treatment related

Emotional & behavioral impact

New Onset

- Depression
- Anxiety
- Adjustment disorders
- HIV mania
- HIV psychosis

Pre-exist / recurrent / comorbid

- Mood disorders
- Substance use disorders
- Other mental disorders

Definiton of HIV associated neurocognitive disorders (HAND)



	Pre-existing Cause	Delirium Absent	Acquired Impairment in ≥ 2 Cognitive Abilities	Interferes with Daily Functioning
Asymptomatic Neurocognitive Impairment (ANI)	No	Yes	Yes	No
Mild Neurocognitive Disorder (MNCD)	No	Yes	Yes	Mild
HIV-Associated Dementia (HAD)	No	Yes	Marked	Marked

Antinori A, et al. Neurology 2007;69:1789–99

Epidemiology of Symptomatic HAND in cART-Treated Patients



Cohort/Study	N	%ANI	%MNCD	%HAD
Canadian OHTN Cohort (2014)	375	35.47	12.53	10.40
Charter Cohort (2014)	1555	35	9.0	2.0
China (Zhao et al., J-Neuro-virol, 2016)	230	18.27	18.26	8.26
Duesseldorf Cohort	1219	28.31	9.57	4.49
England (McDonnell J et al., J Acquir Immune Def Syndr, 2014)	248	13.7	6.5	0.8
Italy (Focà E et al., Int J Mol Sci, 2016)	206	30.6	15	1.5
Korea (Ku NS et al, HIV Med, 2014)	194	52.9	47.1	-
Malawi (Kelly CM et al., PLoS One, 2014)	106	55	15	3.0
Switzerland (Fasel D et al., BMC Psycho, 2014)	30	64	2	0.25

Diagnostic Approach to HAND in Clinical Practice

- You can:
- Screen for the probability of developing HAND (asking key questions)
- Short-Diagnose HAND
- Diagnose HAND
- Monitor HAND

Screening Methods: Results of the Duesseldorf Cohort



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Self Reported Deficits (SRDs) as Screening-Tools for HAND

- Sensitivity = 0,311
- Specificity = 0,781

	No-SRDs	Yes-SRDs	Total
No-Defs	337 (42,6%)	94 (11,9%)	431 (54,5%)
Yes-Defs	248 (31,4%)	112 (14,2%)	360 (45,5%)
Total	585 (74%)	206 (26%)	791 (100%)

Diagnosing HAND



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- Broad Neuropsychological Test Battery
- Imaging Procedures
- Cerebrospinal Fluid (CSF) Analysis

Practical Considerations “Diagnosis”- Risk Factors for HAND?



Disease	Treatment	Co-morbidities	Demographic
<ul style="list-style-type: none"> ● Low CD4 nadir ● High plasma/CSF VL ● Low current CD4+cell count ● HIV-related CNS disease ● Longer duration of HIV-positivity 	<ul style="list-style-type: none"> ● Poor adherence ● ARV interruptions ● Non-optimal ARV regimen ● Low ARV duration- related to treatment failure ● Potential neurotoxicity ● Lower CPE 	<ul style="list-style-type: none"> ● HCV + ● acute CV event ● CV risk factors ● Anemia and thrombocytopenia ● Psychiatric disorder ● Traumatic brain injury 	<ul style="list-style-type: none"> ● Older individuals ● Low education ● Lower socio-economic status ● Lack of access to care ● Poverty

Controversies and/or open Questions



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- Validity of ANI (*Cherner M et al., J Neurovirol, 2007; Gisslèn M et al., BMC Infect Dis 2011*)
- Neuropathogenesis (and associated homogeneity) of milder forms of HAND (*Bai F et al., AIDS, 2017; Kamat A et al, J Acquir Immune Defic Syndr, 2012*)
- Impact of early cART on HAND prevalence in the future
- Impact of comorbidities and ageing (*Goodkin K et al, Lancet HIV, 2012; van den Dries LWJ et al, AIDS Pat Care, 2017*)
- Method inconsistencies in screening for and diagnosing HAND (*van den Dries LWJ et al, AIDS Pat Care, 2017*)
- Lack of biomarkers (*Carroll A et al, F1000Res, 2017; Petersen et al., PLoS One, 2014*)
- **Modified according to Lucette A. Cysique/Sydney, Australia and Sean B. Rourke/Toronto, Canada**

What should be done in clinical practice (1)?

- **Ideal** procedure from a **neurological point of view**:
- **Screening** (asking key questions) every patient when he/she is tested HIV-positive for neuro-cognitive deficits before he/she is put on cART
- **Neuropsychological testing** („diagnosing“) of every patient when he/she is tested HIV-positive before he/she is put on cART
- **Re-screening** patients with a „No-SRDs-**No-Def**s“ or a „Yes-SRDs-**No-Def**s (*over-reporters*)“ constellation once a year after he/she is put on cART and every six months in case he/she is not put on cART for whatever reason
- **Monitoring** („re-diagnosing“) patients with a „No-SRDs-**Yes-Def**s (under-reporters)“ or a Yes-SRDs-**Yes-Def**s constellation every six months under cART or every three months when he/she is not put on cART for whatever reason

What should be done in clinical practice (2)?

- Procedure **proposal** for **non-neurologists**:
- **Screening** (asking key questions) every patient when he/she is tested HIV-positive before he/she is put on cART
- In case of a „**positive screening**“ transmission to a neurologist/neuropsychologist/psychiatrist before he/she is put on cART
- **Re-Screening** every patient who had been „negatively“ screened initially once a year under cART and every six months when he/she is not put on cART for whatever reason
- **Testing for neuro-cognitive deficits** („diagnosing“) of every HIV-positive patient over the age of 50 yrs. with at least two „disease“, „treatment“ and/or „demographic“ risk factors and/or at least one co-morbidity
- **Re-testing** („re-diagnosing“) HIV-positive patients > 50 yrs. with a „risk factor“ constellation every six months

**Thank you for your
attention!**

