Cognitive Performance and Intracerebral Findings in Perinatally HIV-infected Children

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Background

The incidence of severe neurological complications such as HIV-encephalopathy has declined drastically since the introduction of combination antiretroviral therapy (cART).

However, HIV-infection in children is still associated with more subtle neurological and cognitive problems. Of note, studies including matched healthy controls are very scarce.

Magnetic resonance imaging (MRI) may serve as a tool to gain more insight in the mechanisms behind the cognitive deficits.

This study aims to compare cognitive performance and brain MRI parameters of HIV-infected children to age, gender, ethnicity and socioeconomically (SES) matched controls.

Methods

Patients were included from the outpatient clinic of the Emma Children's Hospital AMC, Amsterdam.

Healthy controls were recruited through parental evenings at schools, sports clubs and churches in areas surrounding Amsterdam with a relatively low SES.

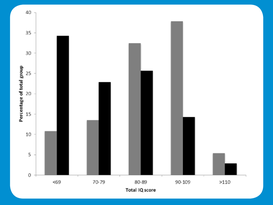
Neuropsychological assessment (NPA) evaluating intelligence, information processing speed, attention, memory, executive- and visual-motor functioning was performed for all participants.

3 Tesla MRI-scan evaluated cerebral structure and microstructure with a T1-weighted sequence, Fluid-Attenuated Inversion Recovery (FLAIR) and Diffuse Tensor Imaging (DTI).

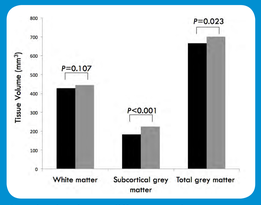
Results

Participant Characteristics

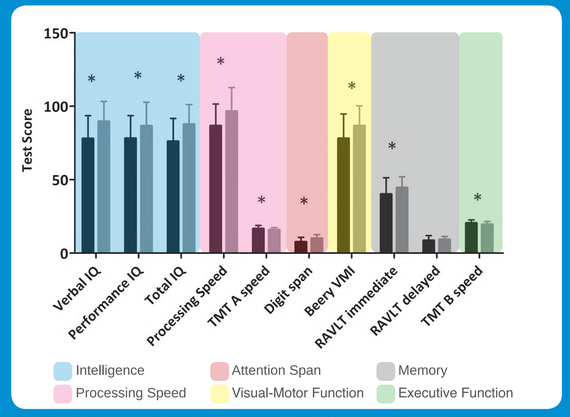
35 HIV-infected children and 37 healthy children
No differences in gender, age and ethnicity
Mostly living in one-parent families (63% vs 68%)
Similar parental education and employment (58% vs 68%)
CDC A: 10 (27%), CDC B: 16 (46%), CDC C: 9 (26%)
History of AIDS in central nervous system: 3 (9%)
Using cART: 31 (89%)



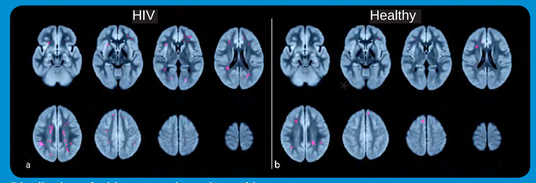
Distribution of total IQ scores in HIV-infected children (black) and healthy controls (grey).



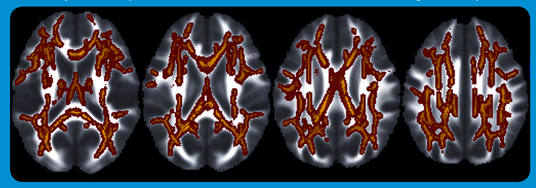
Cerebral volume differences between HIV-infected children (black) and healthy controls (grey). *P*-values adjusted for age, gender and intracranial volume.



Cognitive Performance in HIV-infected children (black) and healthy controls (grey). Abbreviations: IQ=Intelligence Quotient. TMT=Trail Making Test. Beery VMI=Beery-Buktenica developmental test of visual-motor integration. RAVLT=Rey's auditory verbal learning test. *=*P*-value <0.05 (adjusted for age at assessment, gender and parent's educational level)



Distribution of white matter hyperintensities.
a: HIV-infected children (N=16, 59%; mean volume=2.2 cm³, SD=0.7, range 1.2-3.9)
b: Healthy controls (N=6, 18%; mean volume=2.0 cm³, SD=0.3, range 1.5-3.9)



Diffuse pattern of increased mean diffusivity in HIV-infected children as compared to healthy controls. Significantly different voxels (in red-yellow) on the skeleton are projected on the average Fractional Anisotropy.

Conclusions

HIV-infected children performed poorer in all measured cognitive domains (intelligence, information processing speed, attention, memory, executive- and visual-motor functioning), compared with age, gender, ethnicity and SES-matched healthy controls.

A lower grey matter volume was detected in the HIV-infected group, which may represent cortical atrophy.

HIV-infected children had more white matter hyperintensities; of note, these were not absent in the healthy group.

A diffusely spread decreased white matter integrity was found in the HIV-infected group.

Future Directions

The observed cognitive deficits and cerebral injury may influence future intellectual performance, job opportunities and general community participation of the still growing population of HIV-infected children and adolescents. More insight in the observations made by our study is therefore essential, on a patient as well as a population level.

Further studies investigating the underlying mechanisms behind cerebral injury and cognitive deficits in HIV-infected children are warranted, and we intend to explore associations between MRI and cognition, as well as investigate markers of chronic inflammation and neurodegeneration using stored blood and CSF of the HIV-infected participants and blood of the healthy controls.