Differential brain tissue penetration of antiretrovirals and fluconazole

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Background/Methods

• HIV enters the brain within days, leading to neuroinflammation and immune activation → significant neurologic sequelae

• Knowledge of drug exposure in CNS is largely limited to CSF

• Whole blood collected from femoral vein; CSF collected via cisternal puncture; Tissues snap frozen in liquid nitrogen

• Drug quantification performed using high performance (efavirenz) or ultrahigh performance (tenofovir, lamivudine, fluconazole) liquid chromatography coupled with triple quadrupole mass spectrometer

Figure 1: Adapted from Shen et al 2004 and Shannon et al 2013.
Results

- Tenofovir, lamivudine, and fluconazole exposure in CSF over-predicted brain tissue penetration ~7-fold.
- Efavirenz exposure in CSF under-predicted brain tissue penetration between 9- and 14-fold.

Figure 4: Tissue to plasma ratio for Tenofovir (TFV), lamivudine (3TC), efavirenz (EFV) and fluconazole. Median and range of values are reported.
Conclusions

- CSF: plasma ratios were similar to those previously reported in the literature, suggesting minimal impact of post-mortem redistribution but more research is needed.
- Despite good penetration into the CSF, fluconazole penetration in actual brain tissue was low.
- CSF may not be a good surrogate for overall drug exposure in CNS tissues.