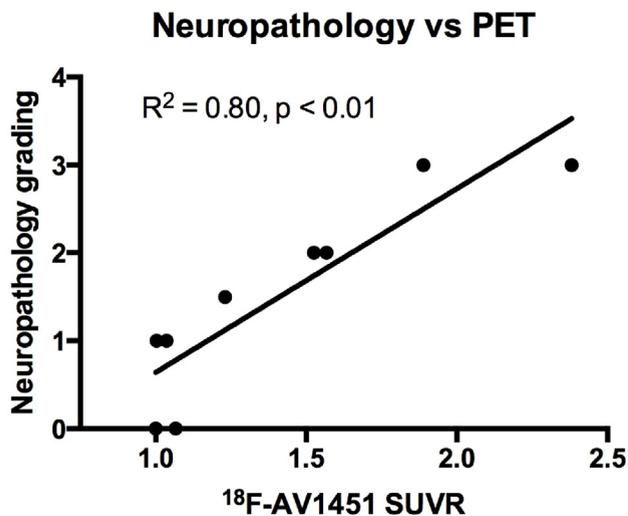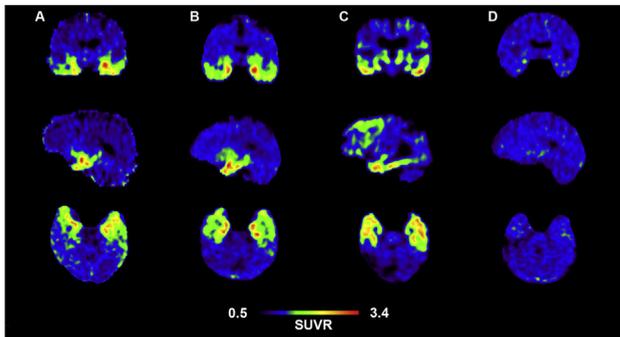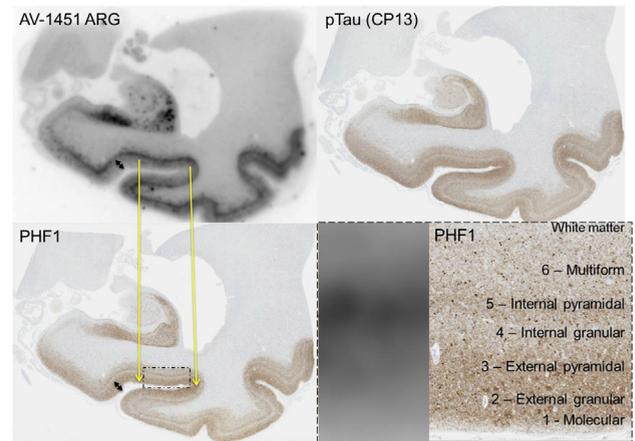scan showed generalised cortical atrophy with a pronounced temporal lobe atrophy and ^{18}F-AV1451 PET imaging revealed uptake in the temporal and frontal lobes, as well as in the basal ganglia (Fig 1 C). The regional uptake of ^{18}F-AV1451 correlated strongly with the tau aggregates revealed using immunohistochemistry ($R^2 = 0.80$, $P < 0.01$; Fig 2). All cases exhibited negative amyloid (^{18}F-flutemetamol) PET scans. **Conclusions:** The *in vivo* uptake of ^{18}F-AV1451 reflects the regional amount of tau aggregates revealed by neuropathological examination. Further, tau pathology in *MAPT* mutation carriers is accurately detected with ^{18}F-AV1451 PET, which consequently can be used to track the effects of anti-tau therapies in this patient group.

Neuropathology vs PET

$R^2 = 0.80$, $p < 0.01$

raphy in autopsy-confirmed Alzheimer's disease (AD) and other neurodegenerative disorders to evaluate the specificity of AV-1451 binding for tau aggregates. **Methods:** Tissue samples were selected that had a variety of dementia-related neuropathologies (n=37). Brain tissue sections were stained for tau, TDP-43, and α-synuclein and compared to adjacent sections processed for AV-1451 autoradiography. **Results:** In AD, AV-1451 preferentially localized to neurofibrillary tangles, with less binding to areas enriched in neuritic pathology. The strength of AV-1451 binding with respect to tau isoforms that preferentially accumulate in various neurodegenerative disorders was as follows: 3R+4R tau (e.g., AD) > 3R tau (e.g., Pick's disease) > 4R tau. Only modest binding of AV-1451 to TDP-43 was detected. No binding of AV-1451 to α-synuclein was detected. "Off-target" binding was seen in vasculature, iron-associated regions, substantia nigra, calcifications in the choroid plexus, and leptomeningeal melanin. **Conclusions:** Reduced AV-1451 binding in AD neuritic pathology compared to neurofibrillary tangles suggests complexity in AV-1451 binding. Maturity of neurofibrillary tangle pathology may play a role. Poor association of AV-1451 with tauopathies that have preferential accumulation of 4R tau or 3R tau suggests that it may have limited clinical utility in detecting these pathologies. In contrast, for disorders associated with 3R+4R tau, such as AD, AV-1451 binds tau avidly but does not reflect completely tau progression suggested by Braak neurofibrillary tangle staging. AV-1451 binding to TDP-43 pathology can be weakly positive in syndromes associated with TDP-43 proteinopathies. Clinical use of AV-1451 will require a familiarity with distinct types of "off-target" binding.

IC-01-05   **NEUROPATHOLOGIC FEATURES OF AV1451 TAU PET AUTORADIOGRAPHY IN DEMENTIA**

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Background: It is essential to determine specificity of AV-1451 PET by using neuropathologic comparisons. We performed autoradiog-

IC-02-01   **THE EFFECTS OF THE TOP 20 ALZHEIMER'S DISEASE RISK GENES ON BRAIN ATROPHY**

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Background: Genome-wide association studies (GWAS) have identified over 20 Alzheimer's disease (AD) risk genes. The mechanism