Examining the neurocircuitry of apathy and markers of neurodegeneration in early Alzheimer’s disease

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Disclosures

• No relevant disclosures
Apathy in Alzheimer’s disease

• Apathy is one of the most common neuropsychiatric symptoms (NPS) in Alzheimer’s disease (AD)
• Apathy is associated with functional impairment and disease progression
• Studies of apathy across multiple neurodegenerative diseases have primarily implicated frontal-subcortical circuitry, but not as clearly in prodromal AD
• **Objective:** To synthesize recent findings from our group examining the association between apathy and markers of neurodegeneration in the early AD spectrum
Regional cortical thinning and apathy in clinically normal elderly and mild cognitive impairment

• We assessed the relationship between apathy measured by the clinician-reported Apathy Evaluation Scale (AES) and regional cortical thickness (structural MRI) in 66 participants (16 clinically normal (CN) elderly and 47 mild cognitive impairment (MCI))

• Results: We found an association between greater apathy and reduced inferior temporal thickness and increased anterior cingulate thickness at baseline

Regional cortical thinning and apathy across the early AD continuum

- We replicated these results in the larger ADNI sample (229 CN, 395 MCI, and 188 mild AD dementia) assessing the relationship between apathy measured by the informant-based Neuropsychiatric Inventory brief questionnaire form (NPI-Q) and cortical thickness at baseline and longitudinally.

- **Results:** We found that inferior temporal atrophy was associated with increasing apathy over time.

Donovan et al. *Am J Geriatr Psychiatry* 2014
NPS and functional connectivity in MCI

• We investigated the association between functional connectivity in four brain networks and NPS using the full NPI in 42 elderly with MCI

• **Results**: We found an association between greater affective symptoms, especially apathy, and reduced frontoparietal control network (FPCN) at baseline

Munro et al. *J Alzheimers Dis* 2015
FDG PET correlates of apathy across the early AD continuum

• We examined the association between apathy using the NPI-Q and FDG metabolism in 402 ADNI participants (104 CN, 203 MCI, and 95 mild AD dementia)

• **Results:** We found that posterior cingulate hypometabolism was associated with greater apathy at baseline

• Supramarginal hypometabolism was associated with increasing apathy over time

Gatchel et al. *Am J Geriatr Psychiatry* 2017
Initial experience with flortaucipir (tau) PET

Apathy and regional tau burden

- We assessed the association between apathy using the AES-C and regional tau burden using flortaucipir PET in 24 participants (13 MCI and 11 AD dementia)
- We explored 9 cortical and subcortical regions
- Regions with unadjusted associations of $p \leq 0.01$ were entered into a model assessing the relationship between tau burden and AES-C
- **Results:** Apathy was associated with greater dorsolateral prefrontal tau burden at baseline
Summary

• We showed that across multiple imaging modalities considered to be proxies of neurodegeneration, apathy in early AD was associated at baseline and over time with frontal-parietal circuitry, as well as the inferior temporal cortex.

• It is unknown if these circuits are intrinsic to apathy, suggested by the frontal involvement, or represent regions typically affected in early AD, suggested by the parietal and inferior temporal involvement, or both.

• Further examination of this question and of the pathologic and neurochemical substrates of apathy will have treatment implications in early AD.
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