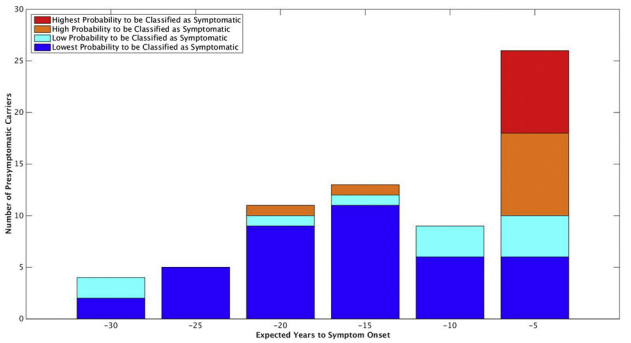
an individual's atrophy pattern was to those observed in the affected carriers. The resulting probabilities were clustered into four groups: from the highest probability (>75%) to the lowest probability (<25%) of being classified as symptomatic. **Results:** Presymptomatic carriers within five years to expected onset were more likely to be classified as symptomatic (Figure). Of the 26 presymptomatic carriers within five years to onset, 16 were classified as symptomatic with a probability greater than 50%. 75% of the presymptomatic carriers in the highest probability group and 37.5% in the next highest group progressed to a global CDR score of 0.5 or greater at a subsequent follow-up scan (range of duration before progression=1.0-4.2 years). Conversely, only one of the ten presymptomatic carriers within five years to expected onset and classified in the lower two probability groups progressed to a higher CDR score at follow-up. **Conclusions:** Atrophy patterns recognised by SVM can provide additional predictive information regarding an individual's proximity to onset. Analysing the complex multivariate patterns in atrophy may help identify whether an individual is truly close to symptom onset or whether their progression is occurring slower than indicated by their expected age at onset.



O1-02-03 EXAMINING LONGITUDINAL NEUROIMAGING PATTERNS IN AUTOSOMAL DOMINANT ALZHEIMER DISEASE: FINDINGS FROM THE DOMINANTLY INHERITED ALZHEIMER NETWORK

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Background: Models of Alzheimer pathology propose that amyloidosis, hypometabolism, and structural declines emerge not only over time, but also spatially in the brain. Autosomal dominant Alzheimer disease (ADAD) provides an elegant way to study the evolution of such pathology due to the ability to stage an individual relative to their years to expected symptom onset (EYO). Longitudinal neuroimaging data is a particularly powerful way to model such changes, as within-subject measures reduces between-subject variability caused by unobserved individual differences. **Methods:** We examined longitudinal PiB, FDG, and structural MRI data in a population of 400 individuals enrolled in the Dominantly Inherited Alzheimer's Network (DIAN). Data were processed examining 34 cortical and 7 subcortical regions. We utilized linear mixed effects models to explore changing pathology. Models were fit for each region included fixed effects for mutation status, time from baseline, baseline EYO, and all possible two and three-way interactions. To allow non-linearities, EYO was modeled as a restricted cubic spline. Analyses were run separately for each modality. The primary focus was on the first time point in the disease where biomarker change in that region differed between mutation carrier and non-carriers. **Results:** Relative to non-carriers, rates of amyloid deposition were significantly higher in carriers at an average EYO across regions of -18.2, glucose metabolism began declining at an average EYO of -14.2, and MRI structural measures declined at an average EYO of -4.2. While this three-stage pattern was common across regions of the brain, it was not ubiquitous (Figure 1). Most prominently a subset of regions demonstrated elevated PiB PET accumulation and structural declines, but not abnormal glucose utilization. Further, the regional timing within a modality (e.g. PiB PET) was highly variable across brain regions (Figure 2). **Conclusions:** Our study presents both the longitudinal temporal trajectories of and spatial patterns of Alzheimer pathology in ADAD cohorts. Our results are consistent with prior theoretical models and cross-sectional work suggesting that initial increases in amyloid accumulation are followed by hypometabolism, and finally by structural atrophy. We demonstrated that there is not one temporal relationship, but that the emergence of pathology varies across the brain.

O1-02-04 CLINICAL RISK RELATED TO CEREBRAL MICROHEMORRHAGES IN AUTOSOMAL DOMINANT ALZHEIMER'S DISEASE: LONGITUDINAL RESULTS FROM THE DIAN STUDY

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Background: Clinical trials of some anti-amyloid treatments have shown increased risks of cerebral microhemorrhages (MCHs) in individuals with Alzheimer disease. These are detectable with gradient-echo (GRE) MR imaging sequences and are part of the constellation of findings defined as amyloid-related imaging abnormalities (ARIA) for which the FDA has recommended monitoring during trials. The presence of 5 or more MCHs has been suggested as a criteria of exclusion from trials. Our aim was to investigate the prevalence of MCHs and their evolution