
**Objective:** To explore the relationship of subsyndromal symptoms of depression (SSD) and MCI considering functional changes, white matter lesions, ApoE status, and progression to dementia. How does SSD impact quality of life in MCI patients?

**Background:**
Major Depression: impacts lifelong disability, co-occurs with neurodegenerative disease, contributes to disability in people with dementia and MCI, risk for institutionalization.
Subsyndromal Depression (SSD): impact on disability less clear than MDD; relationship to white matter lesions (WML) also less clear than MDD.
ApoE: susceptibility gene for AD, relationship of ApoE to SSD not well studied.

**Hypotheses:**
1. SSD in MCI: a) is common; b) will impact disability ratings at baseline; c) will predict poorer course of disability; d) will predict more rapid conversion to dementia over 2 years
2. SSD and biomarkers: a) increase burden in WML; b) WML → disability ratings independent of SSD, APoE, and overall cognitive functioning.

**Methods:**
Uses data from 405 participants in the ADNI study (Alzheimer’s Disease Neuroimaging Initiative) which is aimed at identifying biomarkers of early AD
Inclusion: ages 55-90, diagnosis of MCI
Exclusion: MDD (GDS >6), vascular risk factors, significant neuro or psych illness, certain medication classes

**Measures:**
Disability: FAQ (6 months)  MRI: 1.5T
Sx of depression: Short form of the GDS  WML volume: FreeSurfer software
Cog functioning: ADAS-COG

**Analyses:**
- SSD to demographic and clinical characteristics: Wilcoxon-Mann-Whitney tests and Fischer’s exact tests
- SSD and functional disability and baseline: POLR model
- Change in FAQ over time: generalized estimating equations (GEE)
Results:
• 77% with GDS score between 1 and 5
• SSD were younger and more positive for ApoE4 compared to non-depressed
• SSD had lower WML volumes than non-depressed
• 1.77x more likely to have worse FAQ scores than non-depressed, adjusted for ApoE4 status
• WML and ICV not associated with poorer FAQ scores
• No association between baseline depression type and rate of FAQ change, considering ADAS-Cog scores.
• 44.1% over two years converted to dementia, no difference in SSD vs. non-dementia groups

Discussion:
• SSD is common among MCI participants and is associated with baseline ratings of disability for this population – confirming hypotheses
  o Implication: SSD and minor depression is treatable, possible to avert some functional deficits.
• WML not associated with SSD or with increased burden – not anticipated result
  o Explanation: Could be MDD is associated, where SSD is not as much
• ApoE status associated with SSD
  o Implication: Could have some genetic contribution
• SSD not associated with poorer cost of disability or cog functioning over 2 years
  o Implication: SSD is not a characteristic of higher risk as MDD is.

Limitations:
• Major limitation to the way depression and SSD are characterized.
  o E.g. GDS item 10 – “Do you feel you have more problems with memory than most”
  o No clinical or diagnostic interview to characterize depression
  o Did not evaluate for fluctuations in mood over the 2 year period – development of MDD, changes in SSD status.
• Methodology related to WML volumes