

Simulated Treatment of Agitation in an Alzheimer’s Disease Neuropsychiatric Symptom Network

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Introduction

- Agitation is a common neuropsychiatric symptom (NPS) in Alzheimer’s disease (AD).
- Agitation commonly co-occurs with other NPS.
- There are several clinical trials for treatment of agitation in AD.
- Trials typically measure changes in agitation rather than changes in overall NPS comorbidity following treatment.
- This proof-of-concept study simulates how treatment of agitation could influence a broader NPS network in a biomarker-confirmed AD sample.
- Simulated treatment of agitation should result in reduced network connectivity (H1) and alter network structure (H2).

Methods

Data: National Alzheimer’s Coordinating Center (NACC) Uniform Data Set (UDS)

Participants: Cognitive impairment due to AD; positive amyloid biomarker (CSF and/or PET); endorsed at least 1 NPS

- “Baseline” sample: $n = 1065$; $M_{age}=68.3[9.0]$; 54% female; 80% non-Hispanic white
- “Treatment” subsample: those with MMSE scores= 5-28 ($n = 815$)

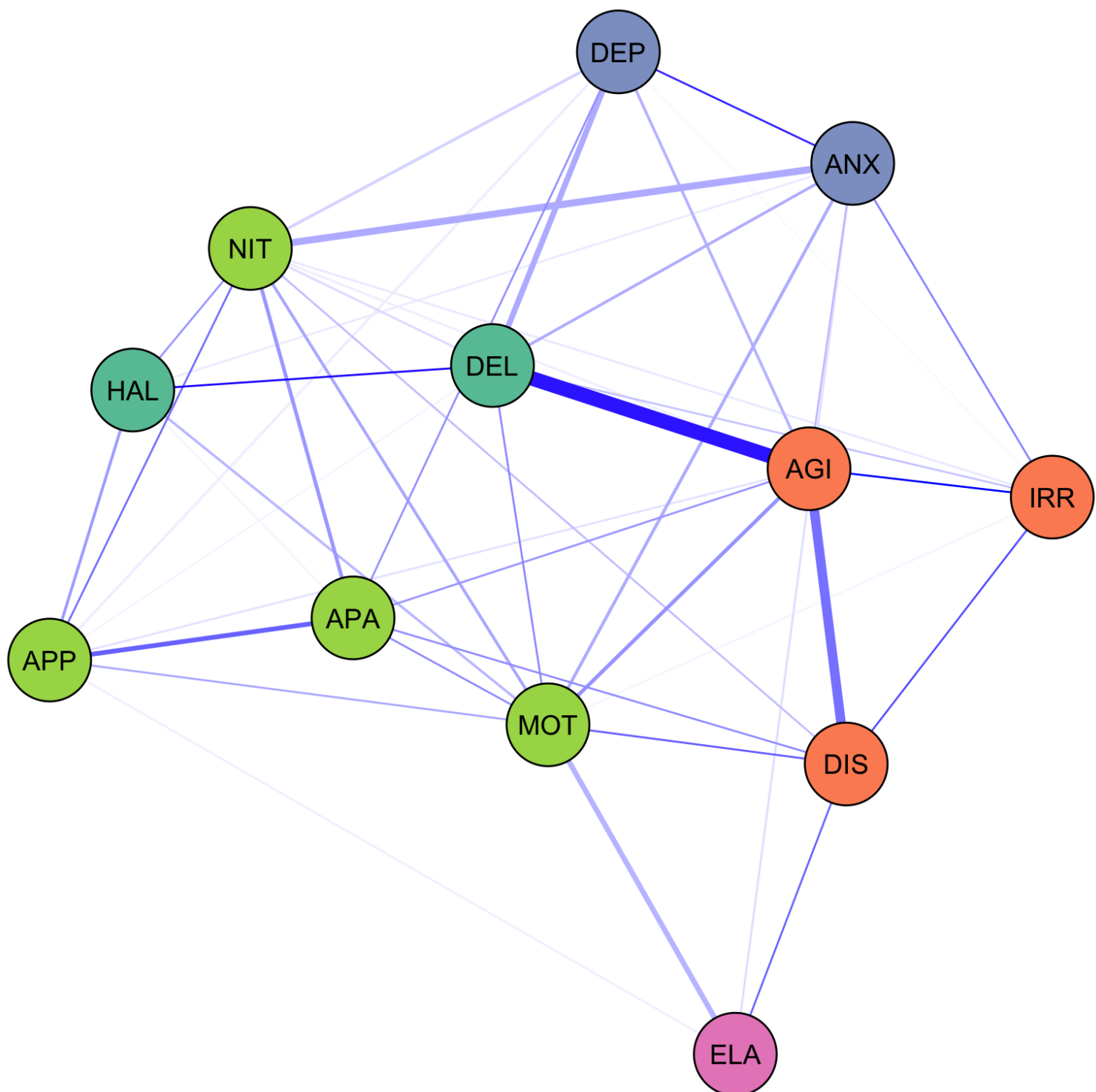
Measure: Neuropsychiatric Inventory Questionnaire (NPI-Q) (12 items)

Analyses: Network analysis of NPS using GLASSO algorithm. Nodes = NPI-Q items.

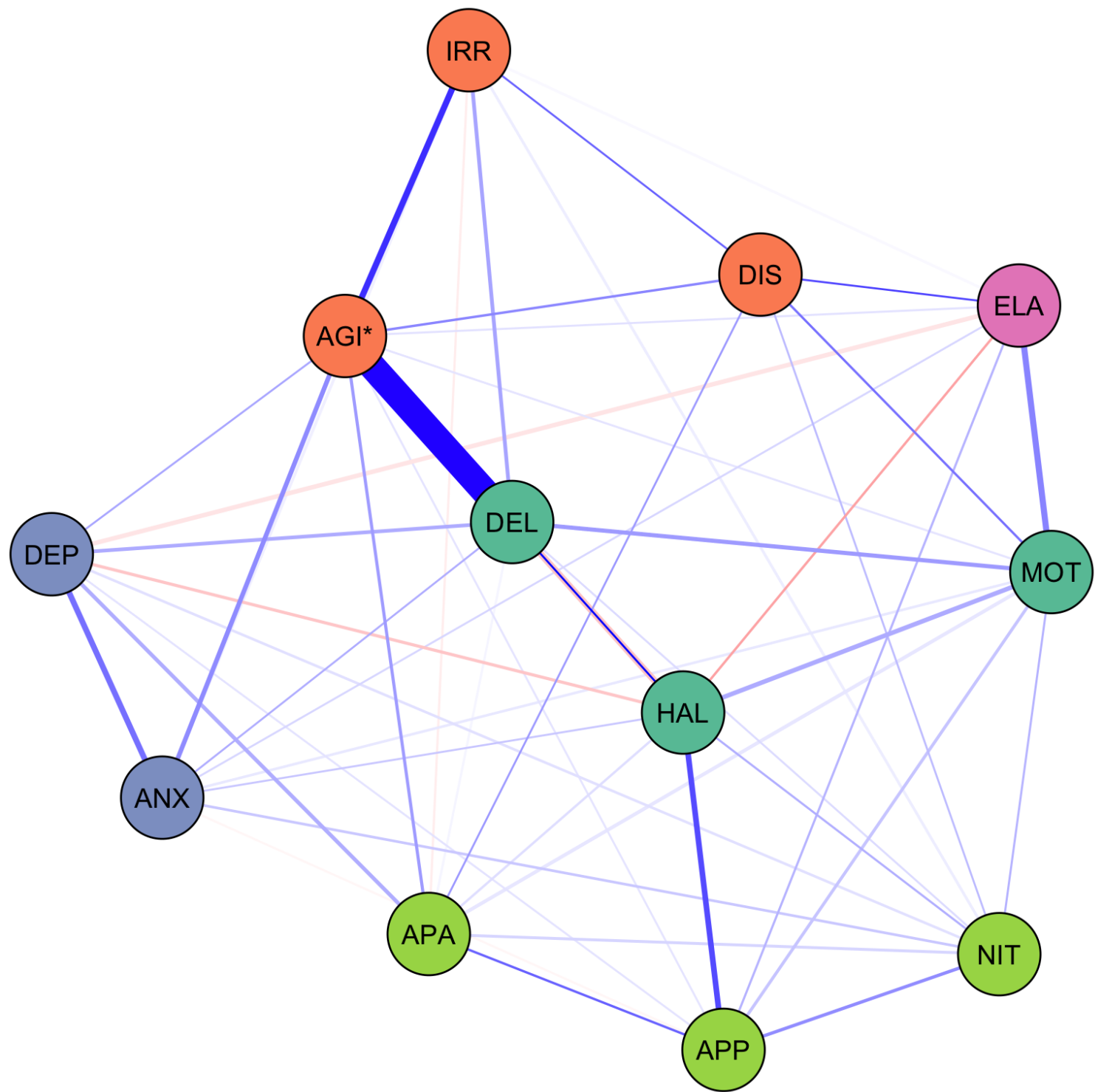
Edges (lines) = associations between nodes.

1. Baseline network was estimated.
2. Treatment subsample received simulated treatment of agitation by recoding agitation scores to reflect improvement (e.g., moderate-severe into mild)
3. Treated network of the 11 original item scores and “treated” agitation item was estimated.
4. Baseline and Treated networks were compared.

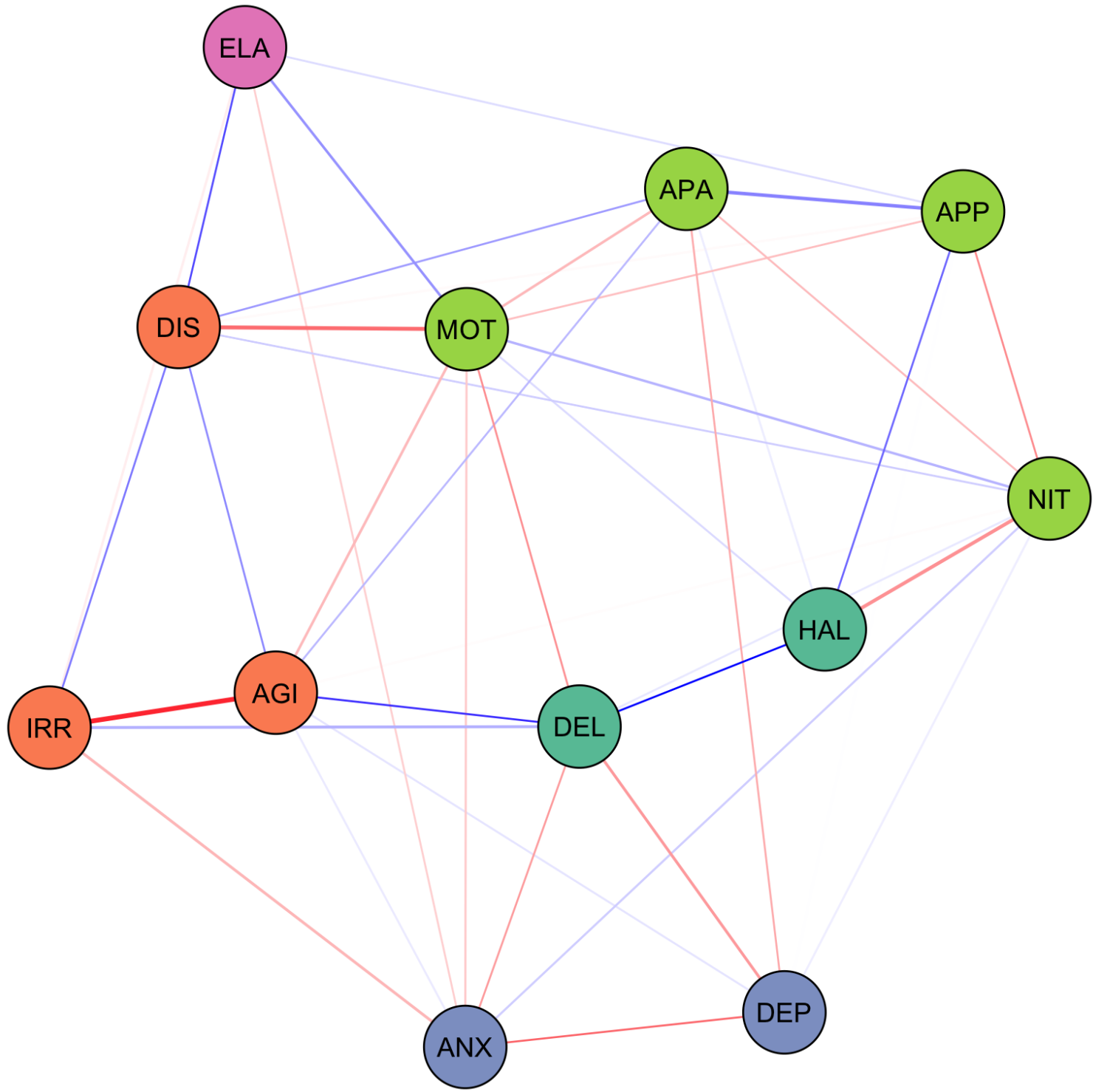
A. Baseline NPS Network



B. Treated NPS Network



C. Difference Network



Note. Symptoms with stronger associations are grouped together with the same color.

Panels A and B: Edges represent statistical association between nodes.

- Blue lines = positive edges
- Red lines = negative edges
- Line thickness = strength of association

Panel C: Edges represent change in edge-weight between Baseline and Treated networks.

- Blue lines = edge became stronger
- Red lines = edge became weaker
- Gray lines = edge remained the same
- Line thickness = degree of change

“DEL” = delusions, “HAL” = hallucinations, “AGI” = original agitation/aggression, “AGI*” = treated agitation/aggression, “DEP” = depression/dysphoria, “ANX” = anxiety, “ELA” = elation/euphoria, “APA” = apathy/indifference, “DIS” = disinhibition, “IRR” = irritability/lability, “MOT” = motor disturbance, “NIT” nighttime behaviors, “APP” appetite/eating problems,

Results

- In both networks, strongest edges connected similar symptoms (e.g., hallucinations and delusions)
- H1: Network changes were observed following treatment
 - 25 edges weakened
 - 27 strengthened
 - 14 remained consistent
- H2: 38% of the edge-weights changed in magnitude following simulated treatment.

Discussion

- H1 was partially supported—simulated treatment of agitation resulted in complex network changes
- H2 was supported—patterns of NPS co-occurrence changed following simulated treatment
- Targeting agitation can have widespread implications on NPS in AD.
- Networks may be useful for outcome monitoring in NPS trials in AD.
- Future work using clinical trial data will clarify treatment effects on symptom severity and comorbidity.

References

