DISTINCT DISRUPTION OF DEFAULT MODE NETWORK FUNCTIONAL CONNECTIVITY IN SEMANTIC DEMENTIA

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Background

- Semantic dementia (SD) is characterized by multimodal loss of semantic memory and anomia, with relative preservation of episodic memory[1].
- Most recent studies convergently implicate SD in dysfunction of default mode network (DMN) functional connectivity[2,3].
- Few demonstrate how connectivity disruptions account for SD deficits[4].

Main objective

- Examine the integrity of DMN activity in SD patients
- Target disrupted DMN components for their relation to SD impairments

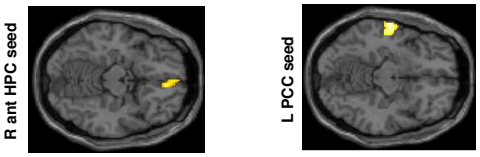
Methods and Design

GIP Cyceron, Caen

- Cognitive measures:
  - Phonemic and verbal fluency (2 min)[5]
  - Semantic attributes task[6]
  - Rey–Osterrieth complex figure delay and copy tasks[7]
  - Doors memory test[8]
- Resting state and structural MRI (3T) : GIFT toolbox, CAT, and SPM12
- Bilateral HPC and PCC coordinates served as seed regions for the connectivity analyses, obtained from literature on DMN:
  - ➢ Right and Left PCC [±8 -56 26] from Andrews-Hannah et al. (2010)
  - ➢ Right and Left antHPC [±18 -14 -18] from Damoiseaux et al. (2016)

Results 1: DMN within network connectivity (p<0.05 FWE)

Hypoconnectivity



R medial orbito-frontal gyrus — L middle temporal gyrus

Peak coordinates for the contrast Controls > SD

➔ Decreased within-DMN connectivity (within right anterior and left posterior components) in SD compared to controls

Conclusions

- The DMN disruptions observed corroborate previous reports of dysfunction in predominantly anterior temporal connectivity in SD
- SD pathophysiology is associated with a disruption in DMN coupling with components of the salience network (SN)
  - ➔ SN recruitment may compensate for overlapping subcortical atrophy[3]
- Semantic impairment is associated with elevated connectivity of temporal DMN seeds
  - ➔ Network reorganization in SD causes dysfunctional shift in DMN hubs
- Functional SD deficits in disrupted DMN-SN coupling and within-DMN hypoconnectivity may mediate the impairments that characterize SD

Participants

- 16 patients diagnosed with SD
- 20 healthy controls matched on age, gender, education, and SES

Table 1 – Demographic and clinical characteristics (mean ± SD) of patients and controls

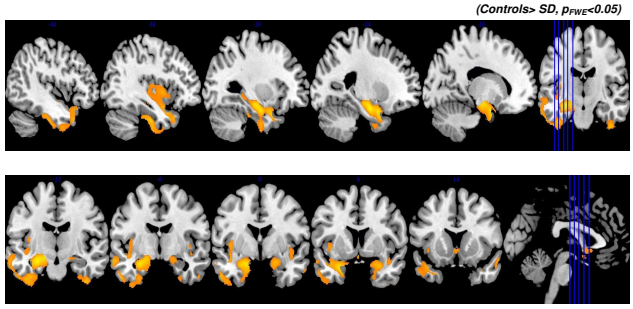
	Patient group (*n*=16)	Control group (*n*=20)	*p*
Age (years)	66.81 ± 6.45	63.25 ± 6.83	*ns*
Education	12.43 ± 3.20	12.1 ± 3.04	*ns*
Gender	11 (9)	6 (10)	*ns*
MoCA Total	20.94 ± 4.56	27.6 ± 1.43	*<.0001*
Letter Fluency	15 ± 7.00	24.35 ± 5.55	*<.0001*
Category Fluency	16.06 ± 8.59	34.85 ± 6.94	*<.0001*
Attribute knowledge	46.19 ± 11.29	53.8 ± 0.41	*<.0001*
Door memory test Total	12.44 ± 4.30	16.7 ± 2.36	*<.0001*
Rey's complex figure task recall	15.25 ± 7.51	21.5 ± 6.62	*<.0001*
Rey's complex figure copy task	34.69 ± 1.49	35.5 ± 0.76	*ns*

MoCA : Montreal Cognitive Assessment[9]; SES: social-economic status

Atrophy Profile in SD

- Characteristic temporal and limbic grey matter loss

(Controls> SD, p_{FWE}<0.05)



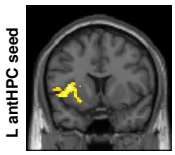
➔ Involvement of bilateral hippocampi, parahippocampal gyri, amygdala, inferior, middle and superior temporal gyri, insula, orbitofrontal cortices and fusiform gyri

➔ Predominantly left lateralized

Results 2: Extra-DMN network connectivity (p<0.05 FWE)

Hyperconnectivity

Peak coordinate for the contrast SD > Controls

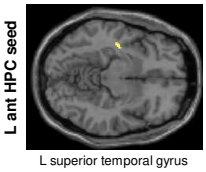


L insula

➔ Increased connectivity with non DMN node in the salience network (DMN-SN) in SD compared to controls

Results 3: DMN correlation with semantic knowledge (p<0.05 FWE)

L ant HPC – L superior temporal gyrus connectivity negatively correlated with semantic attributes



L superior temporal gyrus

➔ Left temporal hyperconnectivity correlates with worse knowledge of conceptual attributes in SD

➔ In line with evidence that the left superior temporal gyrus emerges as central hub of connectivity with increasing severity in SD pathology[2]

References

[1]Gorno-Tempini M. L., Hillis A. E., Weintraub S., Kertesz A., Mendez M., Cappa S. F., et al. (2011). Classification of primary progressive aphasia and its variants. Neurology 76 1006–1014; [2]Agosta F, Henry RG, Migliaccio R, Neuhaus J, Miller BL, Dronkers NF, et al. Language networks in semantic dementia. Brain 2010; 133 ; [3]Farb N. A., Grady C. L., Strother S., Tang-Wai D. F., Masellis M., Black S., et al. (2013). Abnormal network connectivity in frontotemporal dementia: evidence for prefrontal isolation. Cortex 49 1856–187; [4]Yang, Q., Guo, Q.-H. and Bi, Y.-C. (2015), The Brain Connectivity Basis of Semantic Dementia: A Selective Review. CNS Neurosci Ther, 21: 784-792; [5]Cardebat, D., Doyon, B., Puel, M., Goulet, P., & Joanette, Y. (1990). Formal and semantic lexical evocation in normal subjects. Performance and dynamics of production as a function of sex, age and educational level. Acta neurologica belgica, 90(4), 207-217; [6]Desgranges, B., Eustache, F., Rioux, P., de La Sayette, V., & Lechevalier, B. (1996). Memory disorders in Alzheimer's disease and the organization of human memory. Cortex, 32(3), 387-412; [7]Osterrieth, P. A. (1944). Le test de copie d'une figure complexe; contribution a l'etude de la perception et de la memoire. Archives de psychologie; [8]Baddeley, A. D., Emslie, H., & Nimmo-Smith, I. (2006). Doors and people: a test of visual and verbal recall and recognition. Harcourt Assessment;; [9]Nasreddine, Z. S., Phillips, N. A., Bédirian, V., Charbonneau, S., Whitehead, V., Collin, I., … Chertkow, H. (2005). The Montreal Cognitive Assessment, MoCA: A Brief Screening Tool For Mild Cognitive Impairment. Journal of the American Geriatrics Society, 53(4), 695–699.