ACLP

Consultation-Liaison Psychiatry 2022

Hilton Atlanta | Atlanta, GA

NOVEMBER 9-12, 2022

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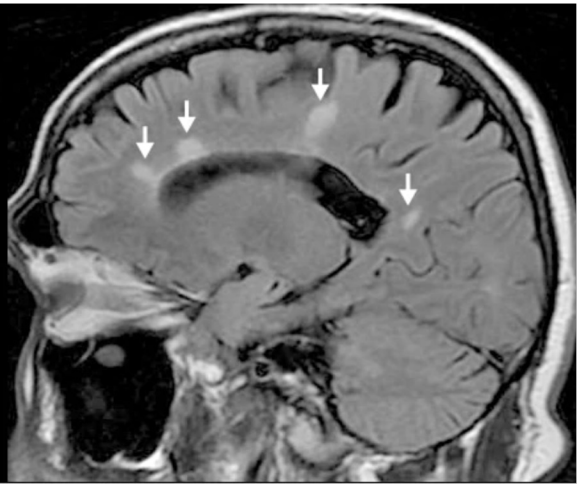
Mapping the relationship between white matter lesions and depression in patients with multiple sclerosis



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NRSA T32 Postdoctoral Fellow

CLP 2022

Disclosure: Erica Baller, MD, MS

With respect to the following presentation, in the 24 months prior to this declaration there has been no financial relationship of any kind between the party listed above and any ACCME-defined ineligible company which could be considered a conflict of interest.

JAMA | Original Investigation

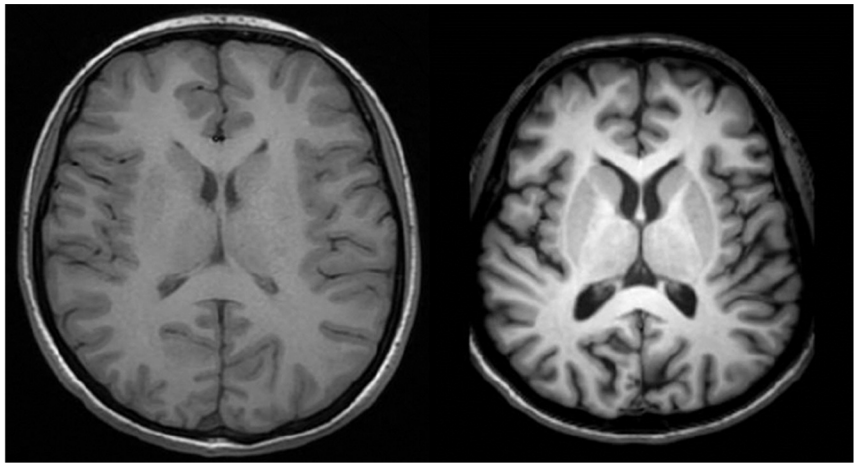
Effect of Sertraline on Depressive Symptoms in Patients With Chronic Kidney Disease Without Dialysis Dependence
The CAST Randomized Clinical Trial

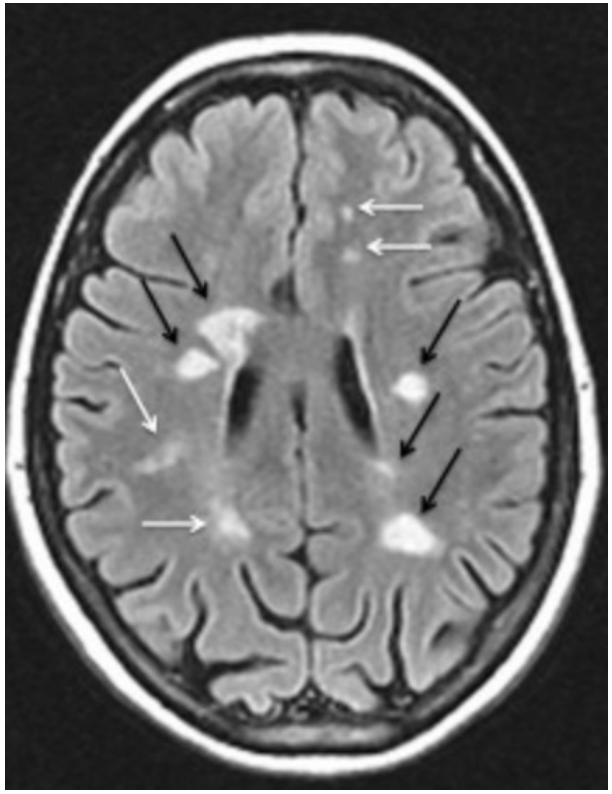
S. Susan Hedayati, MD, MHSc; L. Parker Gregg, MD; Thomas Carmody, PhD; Nishank Jain, MD, MPH; Marisa Toups, MD, MHSc; A. John Rush, MD; Robert D. Toto, MD; Madhukar H. Trivedi, MD

CONCLUSIONS AND RELEVANCE Among patients with non–dialysis-dependent CKD and MDD, treatment with sertraline compared with placebo for 12 weeks did not significantly improve depressive symptoms. These findings do not support the use of sertraline to treat MDD in patients with non–dialysis-dependent CKD.

What I'm interested in - or should I say, what I'm frustrated by

Psychopathology





Current evidence on the efficacy and/or effectiveness of antidepressant medications for MS related depression is lacking. Additional study is needed (Patten and Marrie, 2017).

Multiple Sclerosis and Depression

- 1877: Jean-Martin Charcot noted that people with MS had behavioral irregularities
- 25-50% of people with MS will develop depression
- Rate is 2x-5x higher than general public, also higher than other diseases
- Mood fluctuation may portend relapse

Feinstein et al., 2014

Table 1 | Multiple sclerosis and depression: brain imaging studies

Study	Number of participants	Assessment tools	Imaging modality	Imaging findings associated with depression	Laterality of findings	dings associated sion	Laterality of findings
Sabatini *et al.*[80]	20 (10 depressed. 10 nondepressed)	DSM-III*	Single-photon emission CT	Increased perfusion in limbic areas	Left	rfusion in limbic areas	Left
Pujol *et al.*[67,68]	45	BDI-II‡	T2-weighted MRI	Increased lesion load in the arcuate fasciculus associated with somatic and affective symptoms	Left	sion load in the arcuate ssociated with somatic and nptoms	Left
Fassbender *et al.*[78]	73 (23 with RRMS, 50 healthy controls)	DSM-III-R,* HRSD, ZSRDS	Gadolinium-enhanced MRI	Increased lesion load linked to increased cortisol and a positive dexamethasone suppression test	None reported	sion load linked to increased a positive dexamethasone test	None reported
Bakshi *et al.*[69]	48 (19 depressed, 29 nondepressed)	DSM-IV,* HRSD, BDI	T1-weighted MRI	Superior frontal, superior parietal and temporal lesions; enlargement of lateral and third ventricules; frontal atrophy	Left	ital, superior parietal and ion; enlargement of lateral ntricules; frontal atrophy	Left
Berg *et al.*[72]	78	DSM-IV*	T2-weighted MRI	Increased lesion load in temporal lobe	Right	sion load in temporal lobe	Right
Zorzon *et al.*[71]	90	DSM-IV,* HDRS	MRI	Atrophy in the left frontal lobe; severity of depressive symptoms associated with reduced right temporal lobe volume	Bilateral	e left frontal lobe; severity e symptoms associated with t temporal lobe volume	Bilateral
Feinstein *et al.*[70]	40 (21 depressed, 19 nondepressed)	DSM-IV*	T1-weighted and T2-weighted MRI	Increased lesion volume in medial inferior prefrontal cortex; anterior temporal atrophy	Left	sion volume in medial inferior rtex; anterior temporal atrophy	Left
Passamonti *et al.*[81]	24 (12 with MS, 12 healthy controls)	CMDI, HAM-A‡	Functional MRI	Reduced functional connectivity between ventrolateral prefrontal cortex and amygdala	Bilateral	ctional connectivity between prefrontal cortex and amygdala	Bilateral
Gold *et al.*[75]	49 (20 with RRMS, 29 healthy controls)	BDI-II‡	MRI	Hippocampal atrophy, particularly in CA2, CA3 and dentate gyrus, linked to increased cortisol	Bilateral	atrophy, particularly in CA2, CA3 gyrus, linked to increased cortisol	Bilateral
Feinstein *et al.*[73]	62 (30 depressed, 32 nondepressed)	BDI-II‡	T1-weighted MRI plus diffusion tensor imaging	Increased lesion volume in right medial inferior frontal region; atrophy of left superior frontal region; reduced fractional anisotropy; higher mean diffusivity in left anterior temporal normal-appearing white and grey matter; higher mean diffusivity in right inferior frontal hyperintense lesions	Bilateral	sion volume in right medial al region; atrophy of left superior ; reduced fractional anisotropy; diffusivity in left anterior rmal-appearing white and grey er mean diffusivity in right al hyperintense lesions	Bilateral
Kiy *et al.*[61]	88 (72 with MS, 16 healthy controls)	BDI-II‡	MRI	Increased temporal horn volume correlated with mood-related aspects of the BDI-II, but not with somatic items	Left	mporal horn volume correlated lated aspects of the BDI-II, but atic items	Left
Gold *et al.*[79]	109 women with MS	CES-D‡	MRI	Reduced hippocampal thickness	Right	pocampal thickness	Right

*Participants were diagnosed with major depressive disorder by means of a structured clinical interview. ‡Depression was measured using rating scales, but no formal diagnosis was made. Abbreviations: BDI-II, Beck Depression Inventory; CES-D, Centre for Epidemiologic Studies—Depression Scale; CMDI, Chicago Multiscale Depression Inventory; DSM, Diagnostic Statistical Manual for Mental Disorders; HAM-A, Hamilton Anxiety Rating Scale; HRSD, Hamilton Rating Scale for Depression; MS, multiple sclerosis; RRMS, relapsing–remitting MS; ZSRDS, Zung Self-Report Depression Scale.

*. ‡Depression was measured using rating scales, but no iologic Studies—Depression Scale; CMDI, Chicago ilton Anxiety Rating Scale; HRSD, Hamilton Rating Scale ssion Scale.

No consistent findings

Heterogeneity in

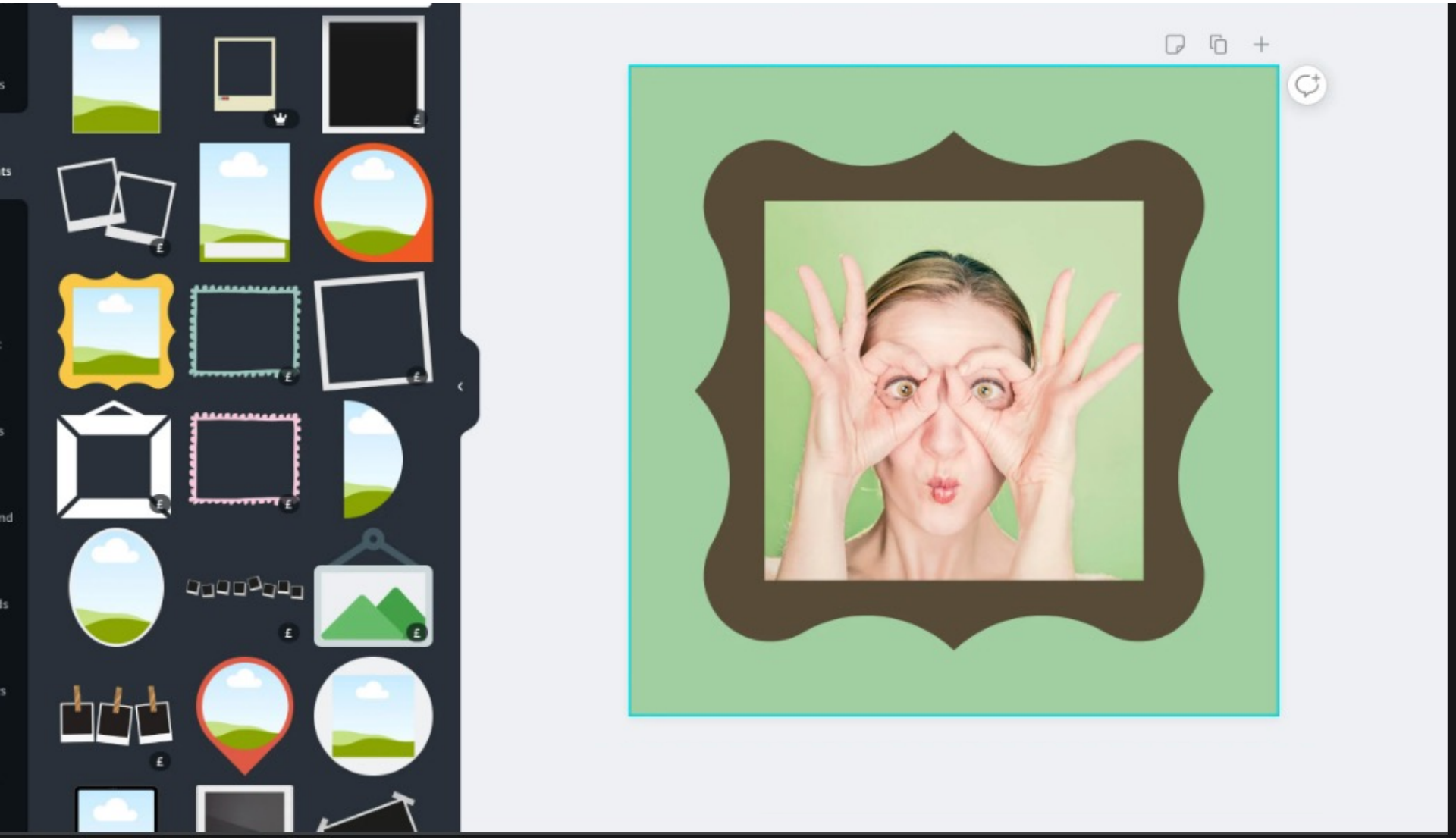
Sample size

Depression screening tool

Imaging Modality

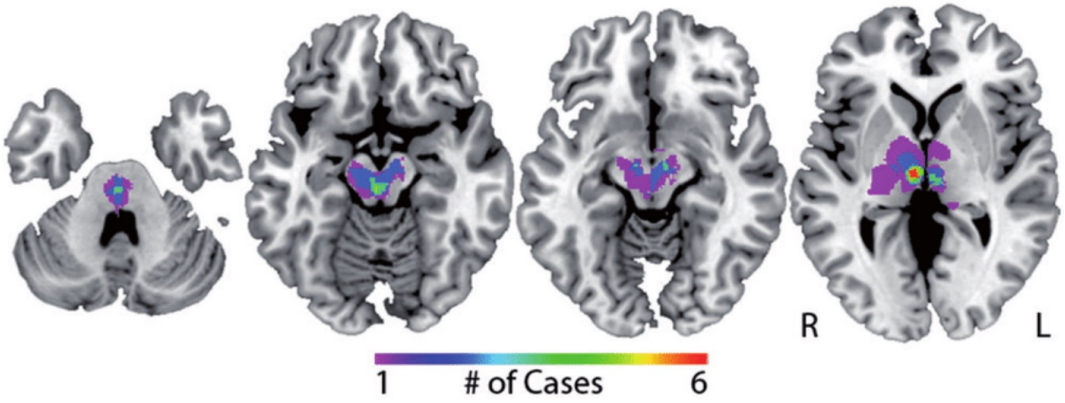
Laterality

Feinstein et al., 2014



Lesion network mapping framework

- Heterogeneous lesions produce similar neuropsychiatric phenotypes
- Create challenges for 1:1 mapping of symptoms to brain
- Hypothesis: Lesions of the same *network* cause similar phenotypes
- Conditions studied so far
  - Peduncular hallucinosis
  - Hemiballismus
  - Depression
  - Delusions
  - Criminality
  - Disorders of free will



Peduncular Hallucinosis Lesions

Boes et al., 2015

Assumption: Functional networks are *structurally connected*

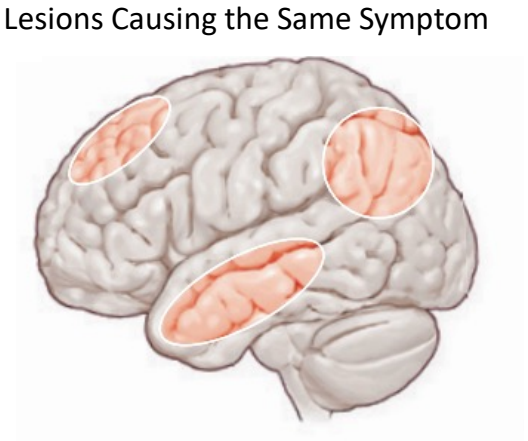
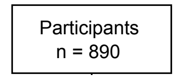


Figure 1. Heterogeneous brain lesions that cause the same symptoms are part of a connected brain network. Adapted from Fox et al., 2018. *NEJM.*

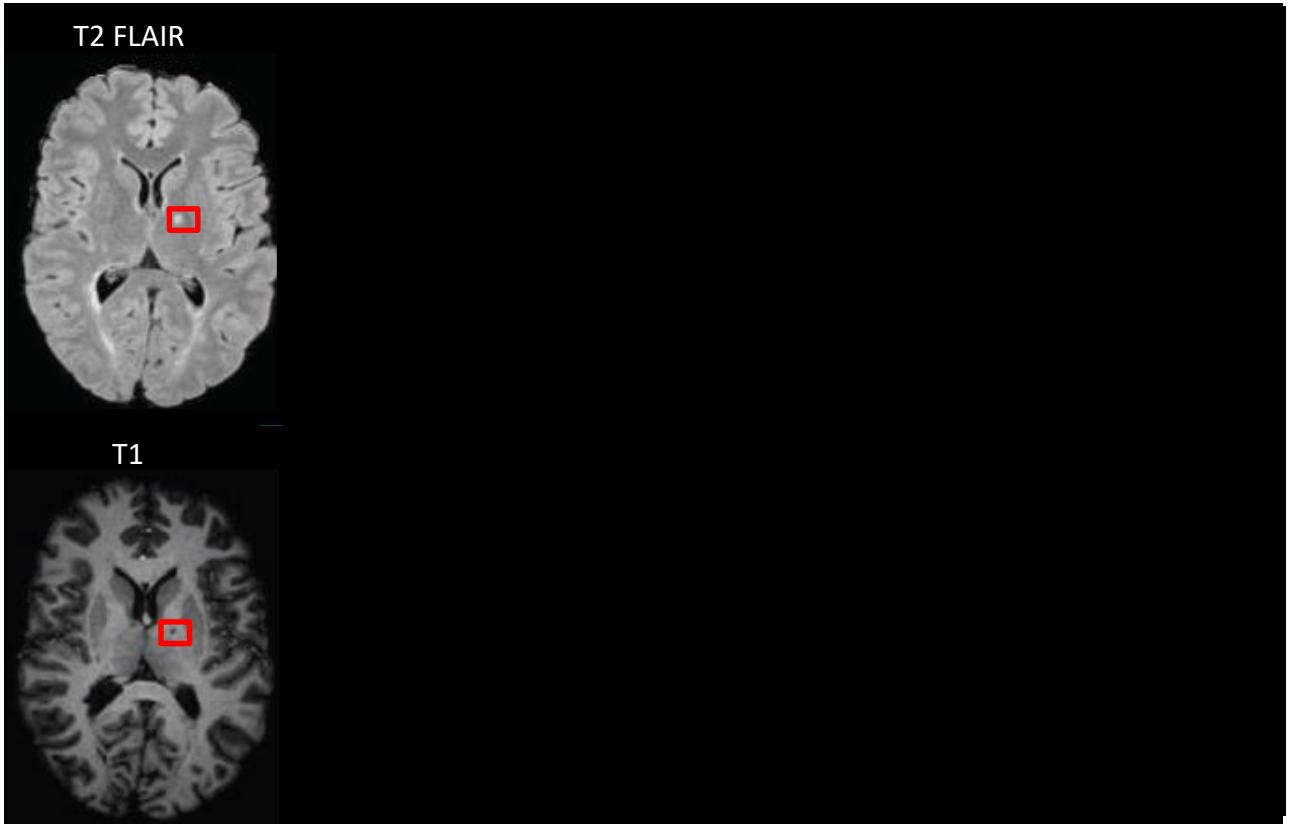
Are white matter lesions in MS that <u>connect</u> these functional networks associated with depression?


Participants
n = 890

Demographics

	MS+Depression	MS-Depression	P
n	232	148	
Age (mean [SD])	48.8 [11.8]	46.6 [12.7]	0.09 (NS)
Sex (% Female)	199 (85.8%)	117 (79.1%)	0.12 (NS)
Race (% White)	173 (74.6%)	108 (73.0%)	0.60 (NS)
PHQ2 (mean [SD])	0.6 [1.5]	0	<0.001
PHQ9 (mean [SD])	10.4 [9.0]	0	<0.001

Automated Lesion Segmentation: Method for Intermodal Segmentation Analysis (MIMoSA)



Valcarcel et al., 2018. *Journal of Neuroimaging*

Assessing white matter fascicle impact from lesions: Streamline Filtering

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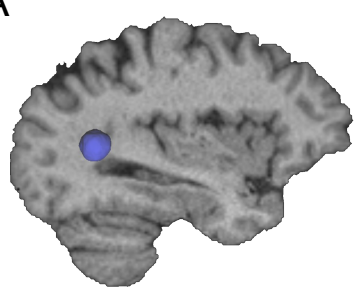

Lesion in native space

Constructing the white matter depression network

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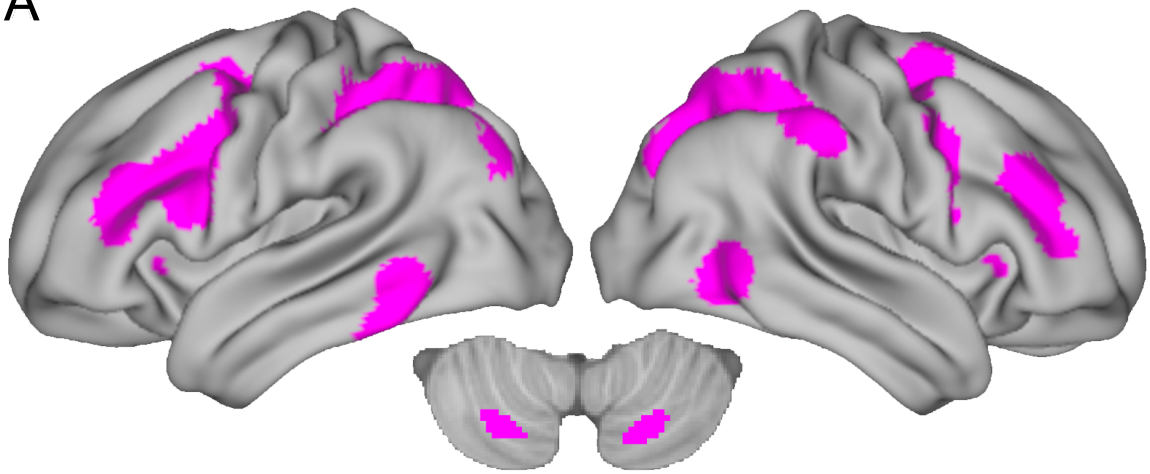
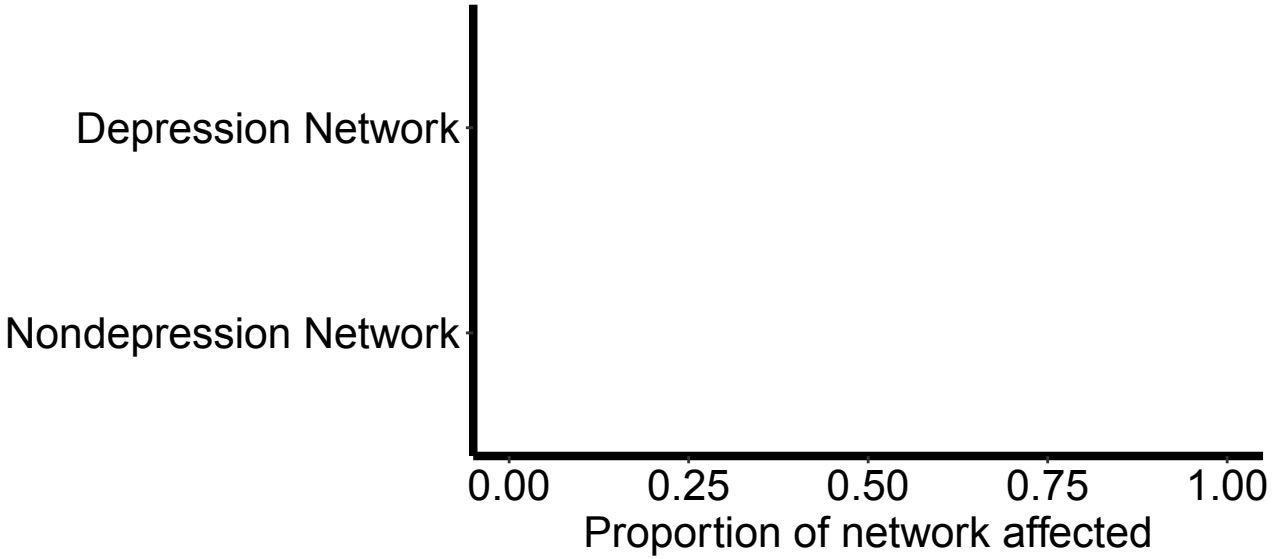
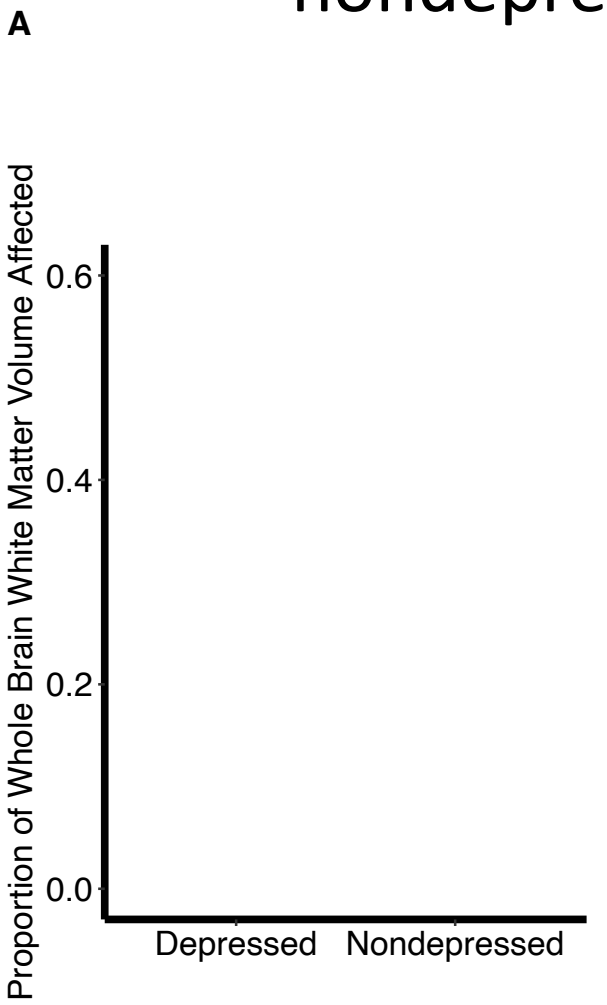


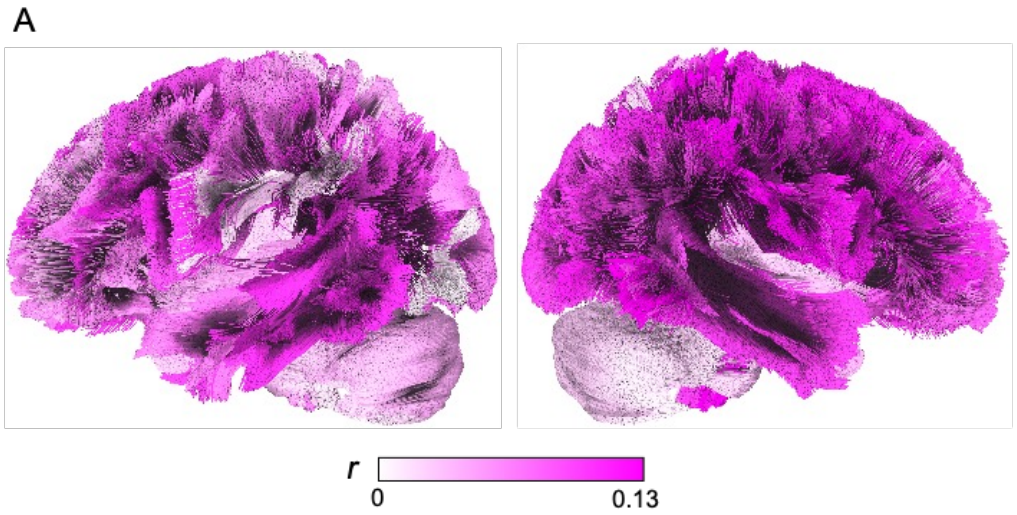
Lesions preferentially impact white matter fascicles in the depression network



Depressed MS patients have more disease than nondepressed MS patients

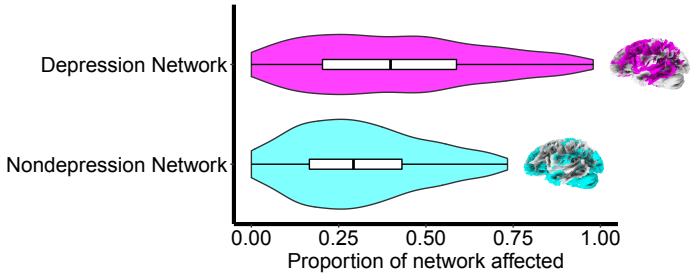


Bigger diagnostic effects in fascicles with higher depression network overlap

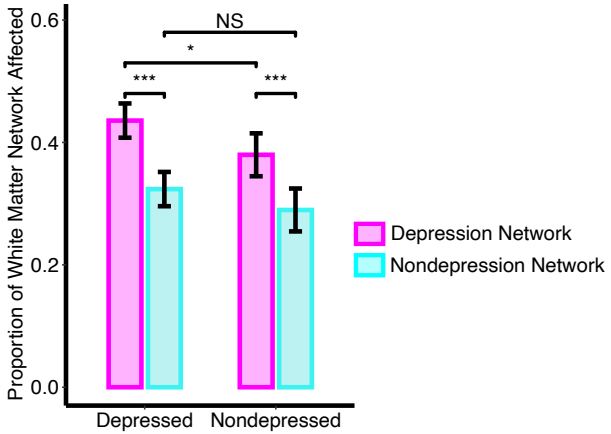


Summary

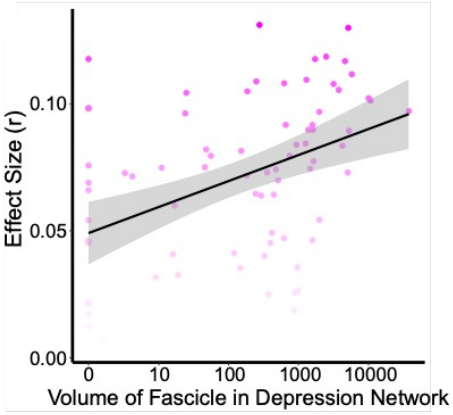
- MS lesions preferentially target white matter fascicles that connect the depression network



- Patients with depression have more disease than nondepressed MS patients
  - Driven by more disease in depression network



- Within each fascicle, bigger diagnostic differences are associated with greater overlap with the depression network



THANK YOU!!!!!

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