

Neural Network Models of Schizophrenia

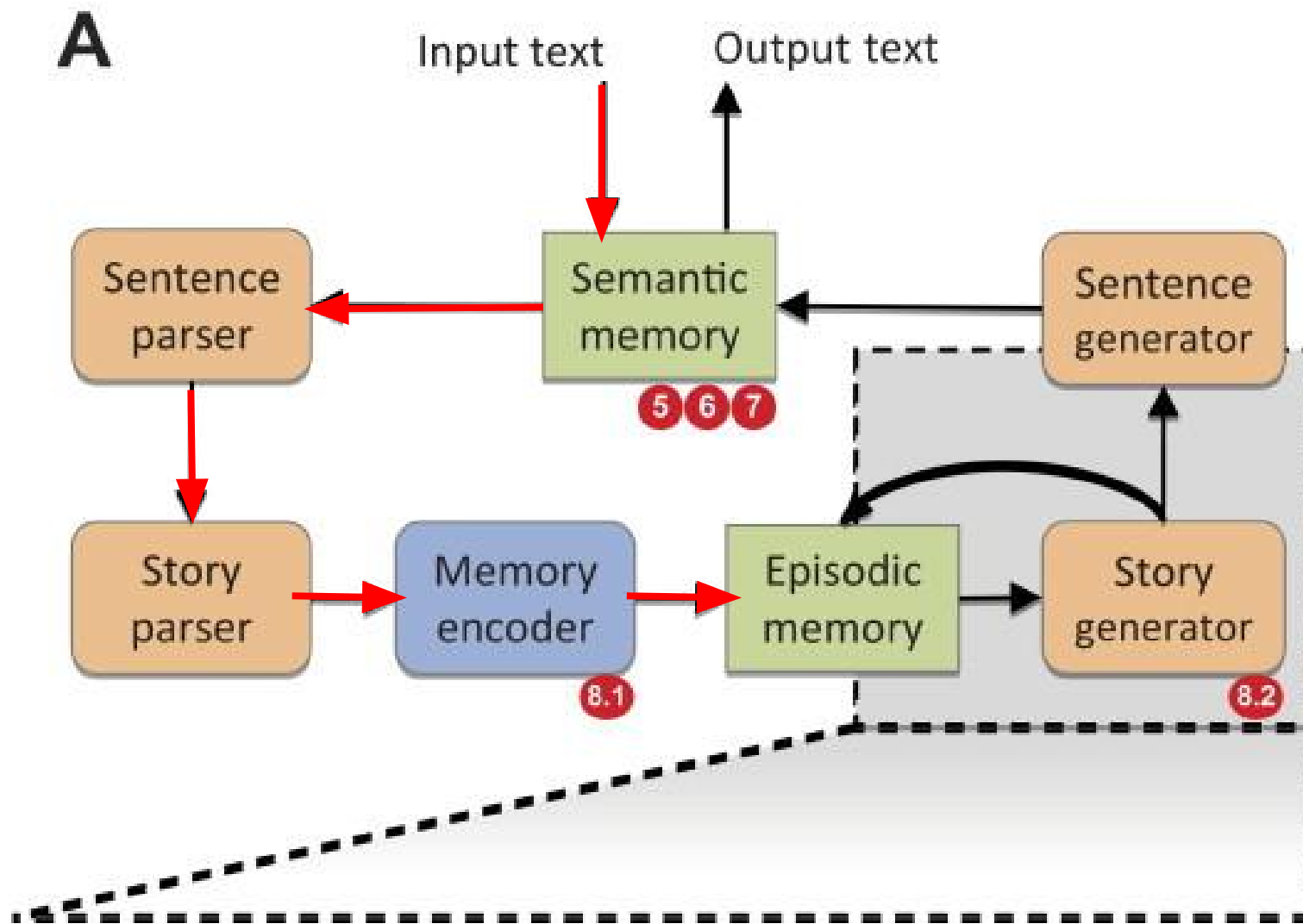
Schizophrenia

Characterized by:

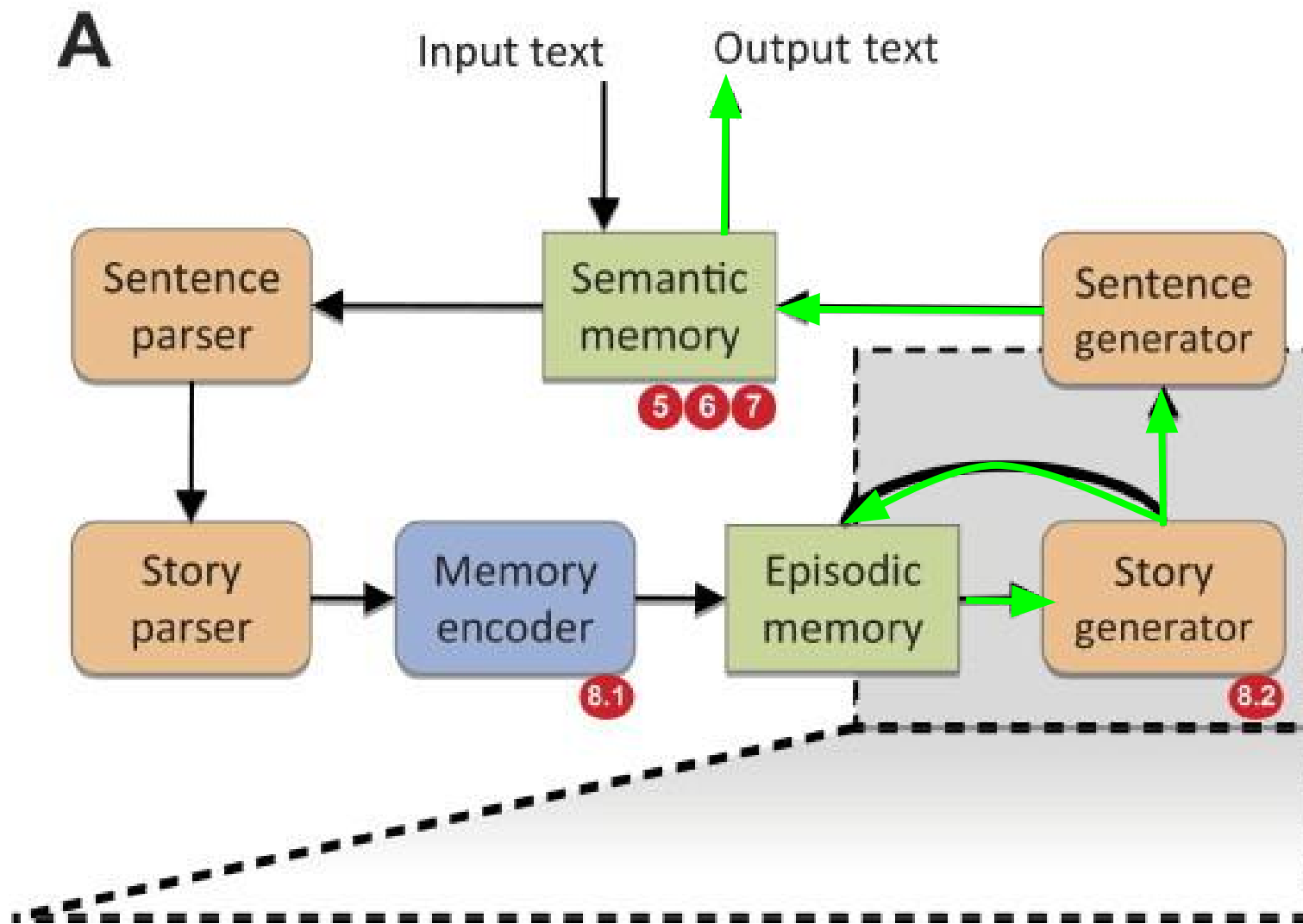
- Errors in spoken discourse
 - Lack of a coherent message
 - Repeated delusions/ spurious narratives
- Auditory hallucinations
- Poor executive functioning
- Disturbed theory of mind
- Reduced dopamine neuromodulation
- Elevated hippocampal activity

DISCERN model for schizophrenic spoken discourse

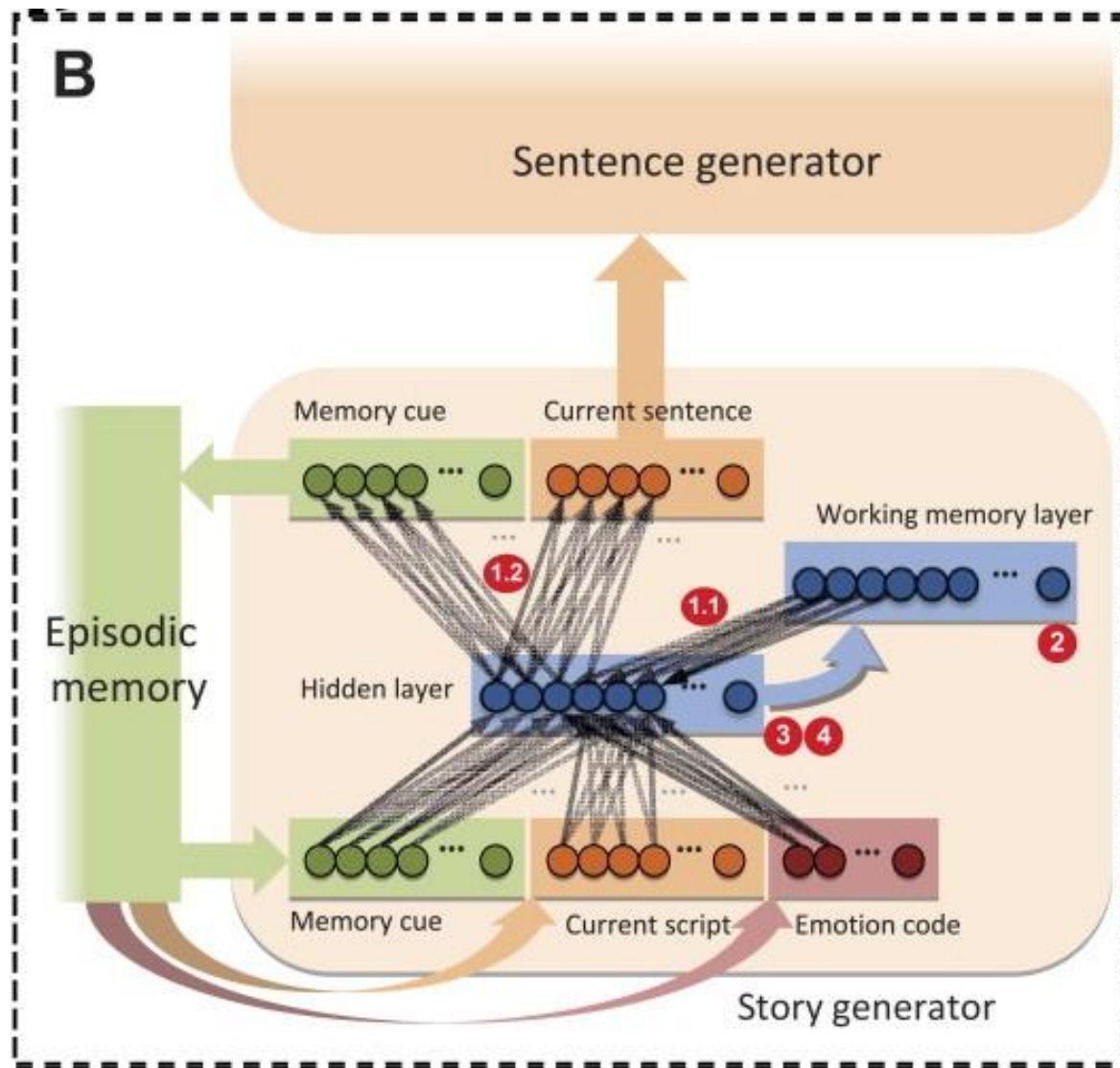
DISCERN model for schizophrenic spoken discourse



DISCERN model for schizophrenic spoken discourse



DISCERN story generator



Scripts and slot fillers

I was a doctor.

I worked in New York.

I liked my job.

I was a good doctor.

Tony was a gangster.

Tony worked in Chicago.

Tony hated his job.

Tony was a bad gangster.

Potential illness mechanisms

- Cortical disconnection especially in working memory
 - Connections in story generator pruned if connection strength too low
- Excessive cortical noise
 - Gaussian noise add to the story generator neurons
- Reduced activation in working memory circuits while performing tasks
 - Reduced “gain,” i.e. slope of the neural response curve
- Elevated arousal on a neural level
 - Shift in response curve, i.e. easier activation of neurons

Potential illness mechanisms

- Distortion of lexical categories
 - Noise added to word representations
- Increased temporal and prefrontal activity during semantic associations
 - Output of neurons in semantic network increased
- Spread of activity during semantic activity
 - Semantic network outputs “blurred”
- Exaggerated prediction-error signaling; “hyperlearning”
 - Additional error-driven backpropagation learning cycles applied

Comparison with human subjects

Subjects (20 healthy, 37 with schizophrenia) were read stories and asked to recite them seven days later.

“The Gift”

In one seat of the bus a wispy old man sat holding a bunch of fresh flowers. Across the aisle was a young girl whose eyes came back again and again to the man's flowers. The time came for the man to get off. He thrust the flowers into the girl's lap. “I can see you love flowers,” he explained, “and I think my wife would like you to have them. I'll tell her I gave them to you.” The girl accepted the flowers and watched the man get off the bus and walk through the gate of an old cemetery.

“Hitchhiker”

I hitched into town. A wispy old man driving a pick-up truck with his frail wife gave me a ride. I sat in the back and watched the tires kick up dust. We stopped and waited for a traffic light. I turned around and peered into the rear window. I hadn't eaten all day and my eyes came back again and again to a bag of Fritos on the dashboard. The man got out of the truck and walked around to the back. “My wife noticed that you kept looking at the Fritos,” he explained, “and she wanted you to have them.”

Quantifying story recall success

Recall success: Normalized number of properly recalled or partially recalled propositions

Proposition List	Subject Recall: "I remember a whispering man that had flowers on a bus and he saw a girl and she wanted them ... "
(i) A (man) sat in a seat on the bus	1 ("man on a bus . . . ")
1. a man rode or is on a bus	
.5. there was a man in some sort of vehicle	
(ii) man was a wispy/old	0
1. old man + indication of frailty	
.5. old man or frail man	
(iii) (man) was hold a bunch of flowers	1 ("[man] had flowers")
1. (man) possessed<comma> holding or carrying flowers	
.5. (man) possessed something	
(iv) A young girl was/sat across the aisle from the man	.5 ("he saw a girl")
1. female sitting next to<comma> near<comma> or across from man	
.5. female riding in the same vehicle as man	
(v) The girl's eyes came back again and again to the man's flowers.	.5 ("[girl] wanted [the flowers]")
1. female paid special attention to the flowers	
.5 female noticed or wanted something	

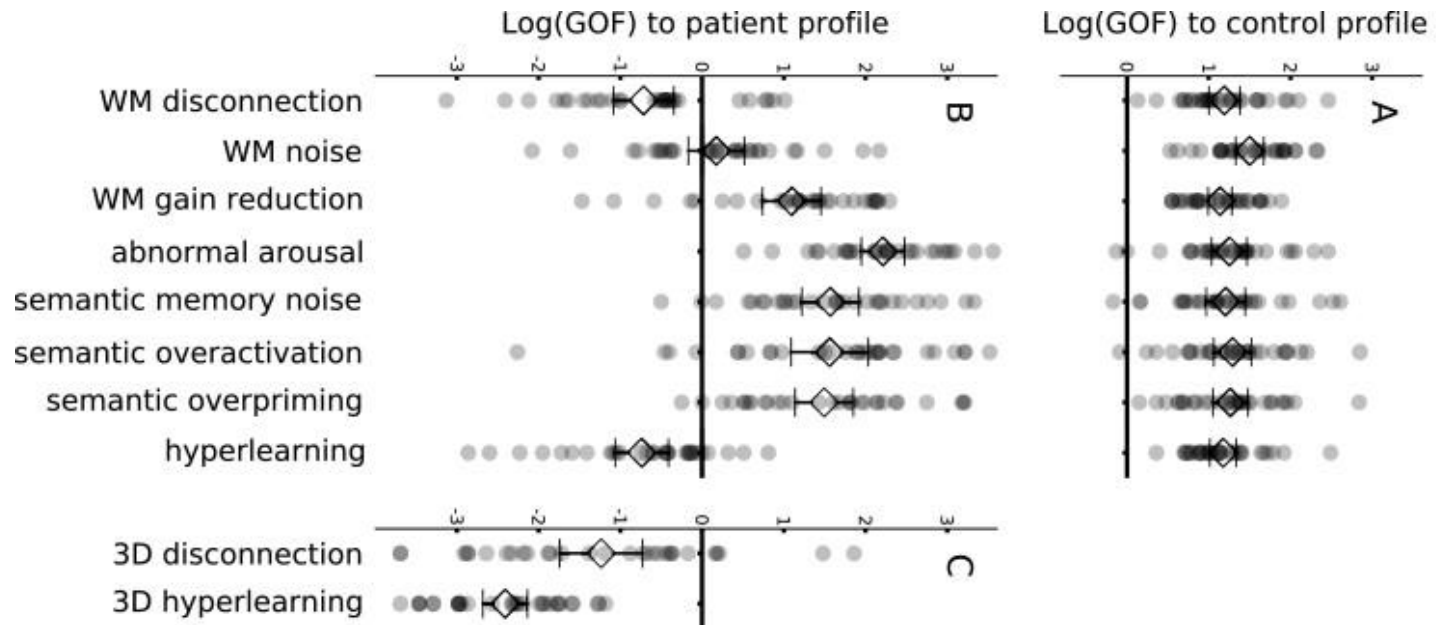
Quantifying story recall success

Types of errors:

- Agent slotting errors
 - Human: “the girl gave the old man the flowers as a gift”
 - DISCERN: “the cop arrested me” (as opposed to Tony)
- Lexical misfire
 - Human: “wispy old man” → “whispering old man”
 - DISCERN: “I was interested in guns” (as opposed to books)
- Derailed clauses
 - Human: “I remember the generosity of the flowers. I remember that he gave her flowers and she gave, she put the flowers on the tombstone. And I remember there was a truck involved, I believe it was a flatbed.”
 - DISCERN: “Joe was my boss. I hated Joe. Joe was in his 30s. Joe had a beard. Joe liked baseball. Mary was the fiancée of Joe. I liked talking to Mary. I gave a kiss good-bye to Mary.”

Results

	Recall Success	Agent Slotting Error Penetrance	Lexical Misfire Penetrance	Derailment Penetrance
Healthy Control Subjects (n = 20)	.67 (.12)	.023 (.033)	.051 (.064)	.011 (.040)
Persons with Schizophrenia (n = 37)	.41 (.23)	.086 (.121)	.065 (.085)	.122 (.226)



Hoffman, Ralph E., Uli Grasemann, Ralitzza Gueorguieva, Donald Quinlan, Douglas Lane, and Risto Miikkulainen. "Using Computational Patients to Evaluate Illness Mechanisms in Schizophrenia." *Biological Psychiatry* 69.10 (2011): 997-1005.