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Brain Maps Define Diseases

Researchers have identified well-delineated brain networks that are linked to five distinct neurodegenerative diseases, according to a paper published in *Neuron* today (April 15).

“I think our data gives researchers a road map -- hopefully a treasure map -- saying this is where we should be looking” when studying both neurodegenerative diseases and cognition in non-diseased brains, said William Seeley; a neurologist at the University of California, San Francisco, Medical Center.

It's well known that different neurodegenerative disorders preferentially target specific regions of the brain. “The reason for that,” explained Marsel Mesulam, a neurologist at Northwestern University in Chicago, “is that different parts of the brain have different properties” on a chemical and immunological level. “The diseases are in some way recognizing that.”

The idea that damage in one part of the brain can affect other areas connected to that region has been around for more than a century, said Mesulam, who was not involved in the new study, but who wrote an accompanying commentary. The study's contribution, he said, is to map out these areas with the help of neuroimaging. “This is an elegant demonstration of a concept that has been around for some time.”

Seeley and his colleagues used fMRI to compare brain activity in healthy control subjects to that

in patients with one of five neurodegenerative diseases with relatively early onsets: Alzheimer's disease, behavioral variant frontotemporal dementia, semantic dementia, progressive nonfluent aphasia, and corticobasal syndrome.

“The surprise element is really how tight the correlation is” between the specific disease and the brain network it activates, said Seeley. In patients with each type of disorder, the brain scans revealed a signature of deficits in functional activity and anatomical structure in distinct areas of the brain.

After identifying networks specifically affected in each disease, the researchers also examined the volume of cortical grey matter in these networks in healthy subjects. They found that different networks were associated with differences in cortical volume, suggesting these interconnected brain regions were functionally related in healthy brains as well.

Focusing on disease “networks” will allow researchers to broaden their study of neurodegenerative disorders beyond the current focus on the pathology within individual cells, Seeley noted. “In my view, a general problem that researchers aren't tackling enough in neurodegeneration is the problem of why the disease finds itself in only specific areas of the brain, and what it is that spreads the disease along specific regional pathways,” he said. “Patients don't get sick because a cell is dying -- it probably isn't even until you get to the network stage that symptoms even start to emerge.”

He believes that the network approach could also provide an early method of diagnosis -- a pervasive problem in the neurodegenerative disease. “The next wave of studies will be to see if network connectivity and function can help us sort patients according to diagnosis,” he said.

Mesulam added that a network approach not only sheds light on neurodegenerative disease, but also can help define how different elements of cognition work together in healthy brains. “If you were able to fully understand how disease A interferes with network B, you would learn a lot about network B,” he said.

But while neuroimaging using functional MRI is a start, Mesulam writes in his commentary, it doesn't sufficiently reveal the anatomy of neuronal connections. To map connections with the

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degree of detail necessary, he writes, will require intensive collaborations between cognitive neuroscientists, physiologists and anatomists and the development of new mapping techniques.

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