



fellowship project

the molecules of behavior

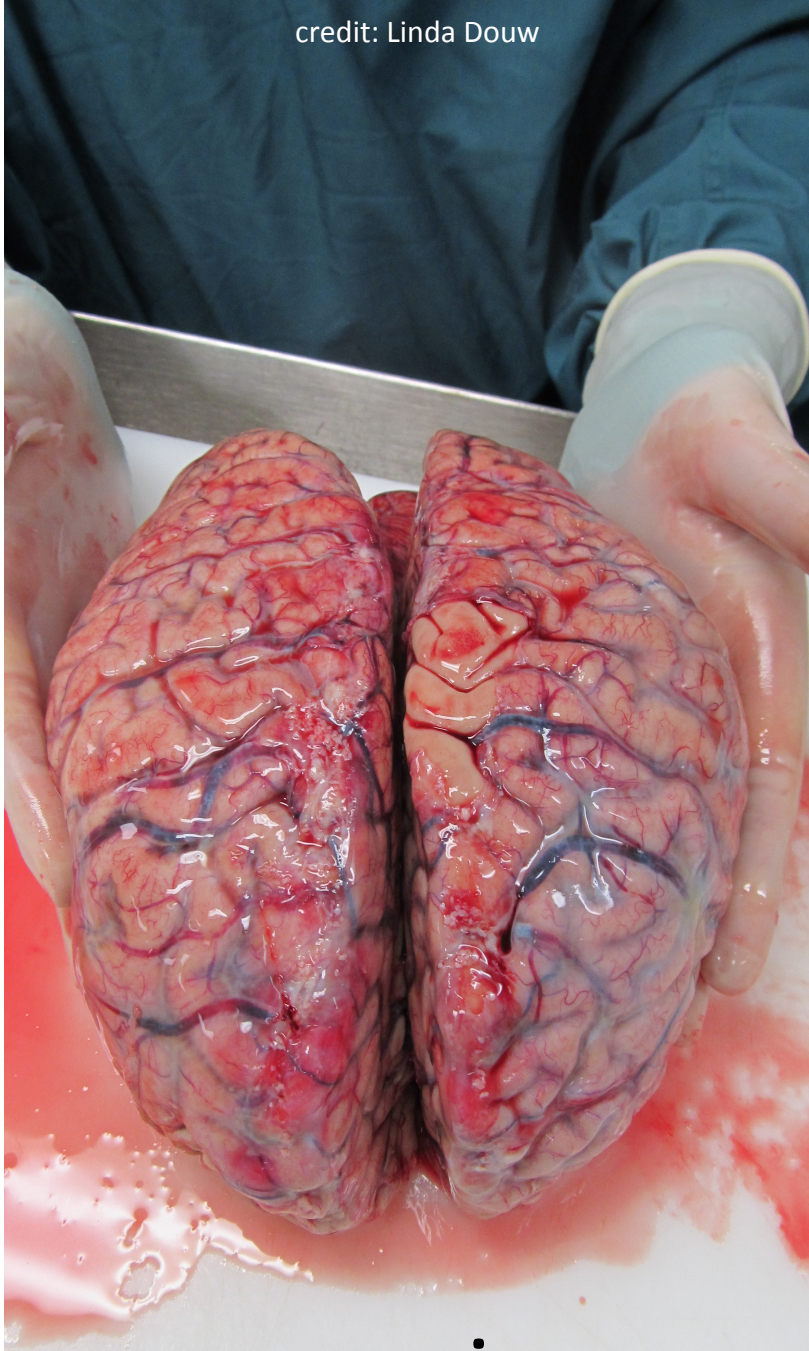
how brain tumors link cellular biology to
large-scale brain networks and cognition

today's title

time, space and scale
in the brain connectome
tying it all together

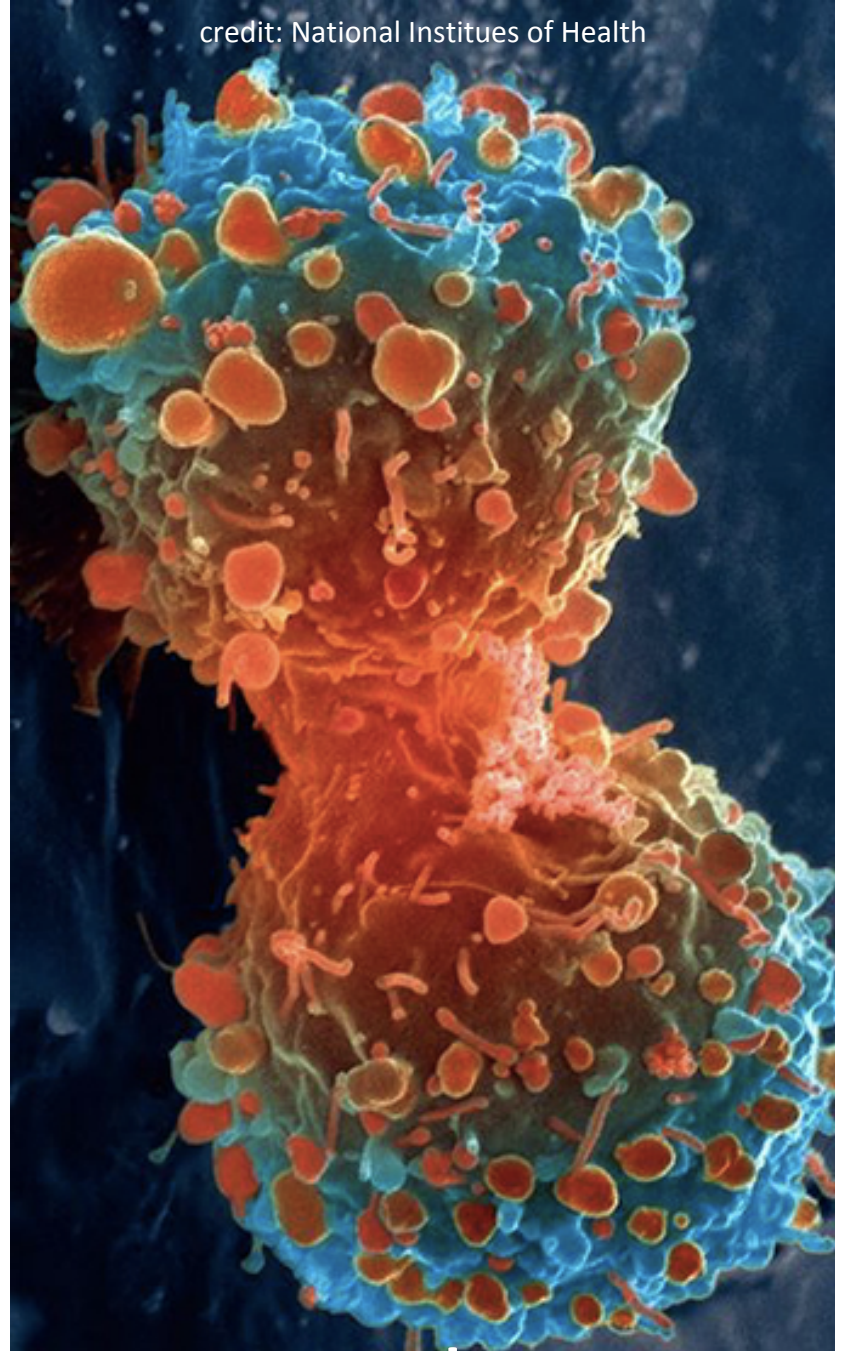
linda douw

credit: Linda Douw



neuroscience

credit: National Institutes of Health



oncology

glioma

primary brain tumor

incidence 7-19/100,000

median survival 14 m – 9 y

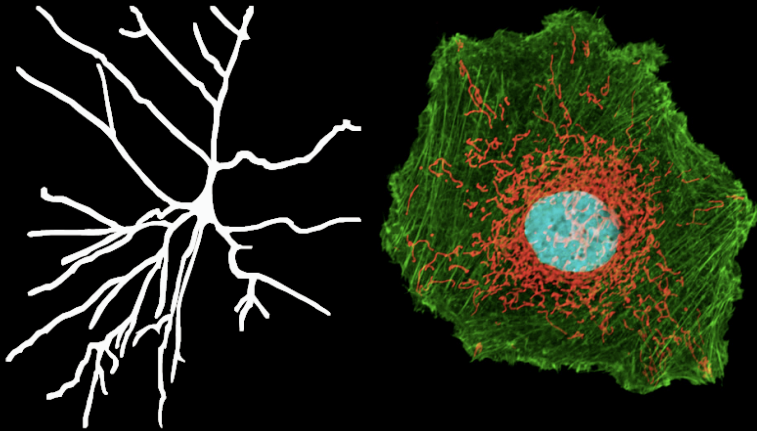
100% mortality rate

poorly understood cognitive deficits

“molecules”

≈

neurons and/or
glioma cells



“behavior”

≈

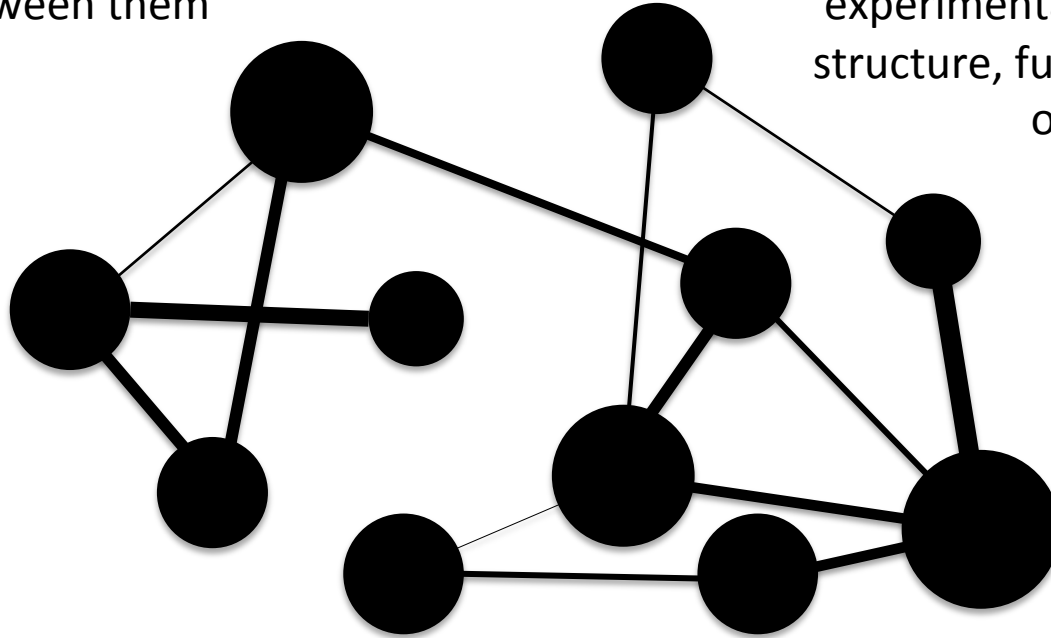
cognition



graph theory

1 | deals with any system that can be represented by nodes and connections between them

2 | well-vetted theoretical and experimental knowledge on the structure, function and dynamics of systems



3 | unifying theory that may facilitate (clinical) neuroscience

the brain network or 'connectome'

- 4 | hubs and their connections are also most dysfunctional when cognitive deficits occur in disease

derks et al (2017) neuroimage clinical;
meijer et al (2017) neurology

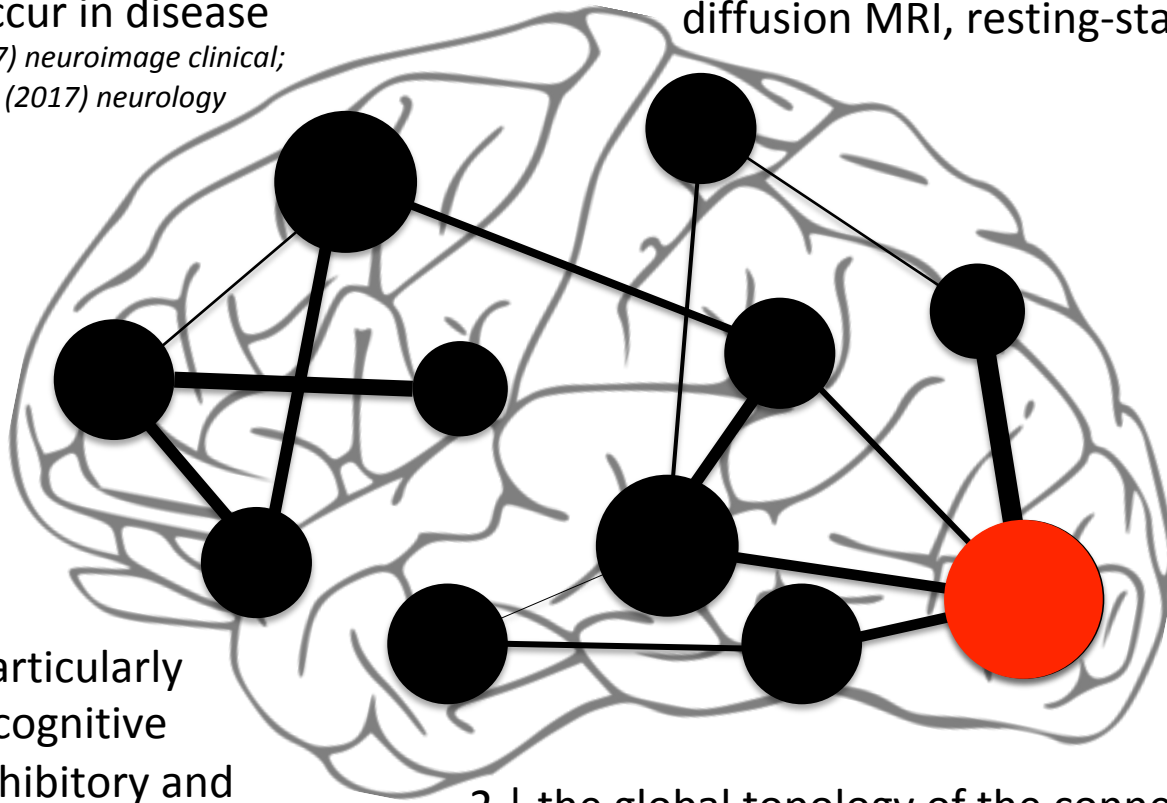
- 1 | can be measured in humans using non-invasive macroscopic techniques like diffusion MRI, resting-state fMRI, EEG, MEG

- 3 | hubs are particularly conducive to cognitive impact of both inhibitory and excitatory perturbation

fitzsimmons et al (under review);
quaak et al (in preparation)

- 2 | the global topology of the connectome correlates with cognitive (dys)function in health and disease and may become a predictive marker of decline

carbo et al (2017) scientific reports

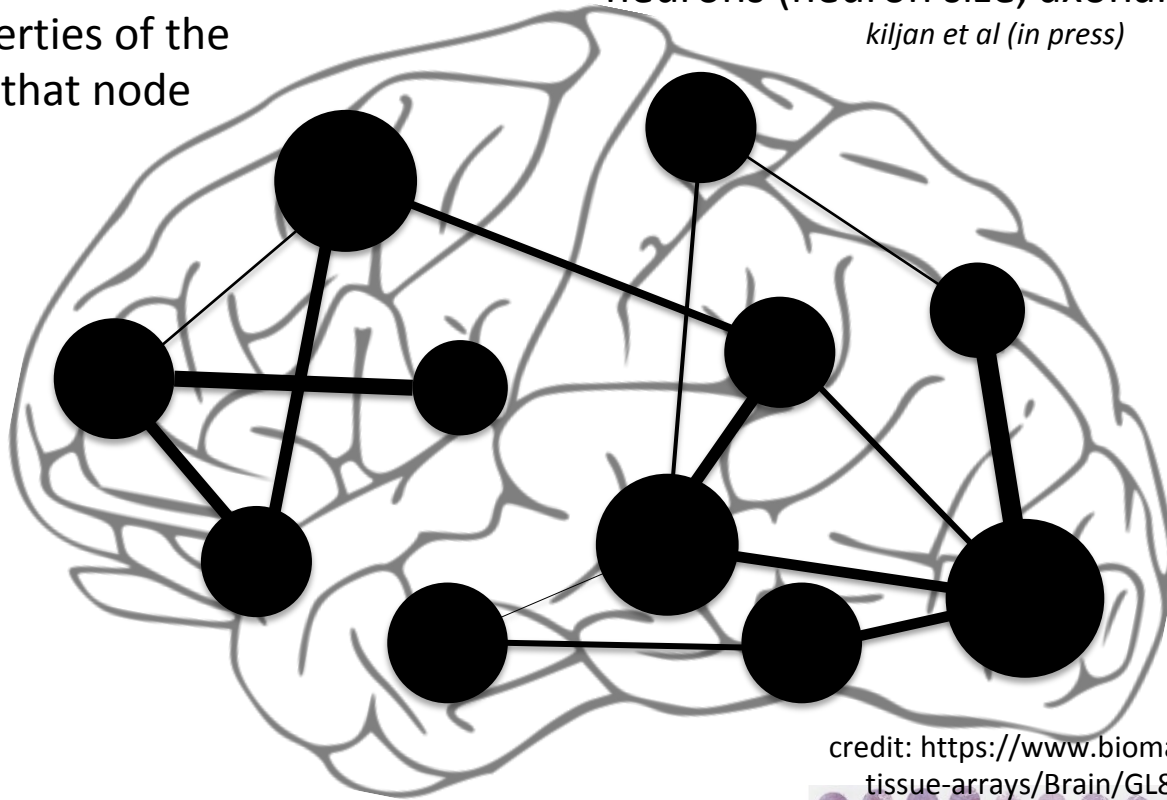


the unique window of opportunity

2 | translate macroscopic nodal properties to microscopic properties of the neurons within that node

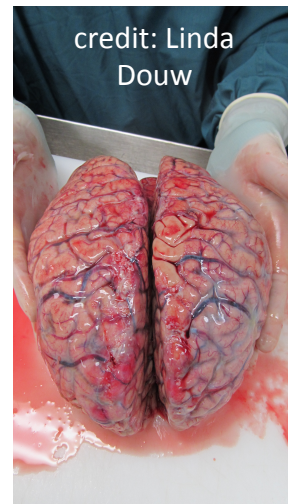
3 | macroscopic hubness correlates with morphology of neurons (neuron size, axonal density) ...

kiljan et al (in press)



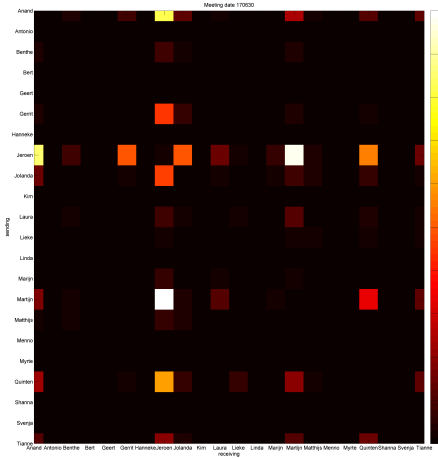
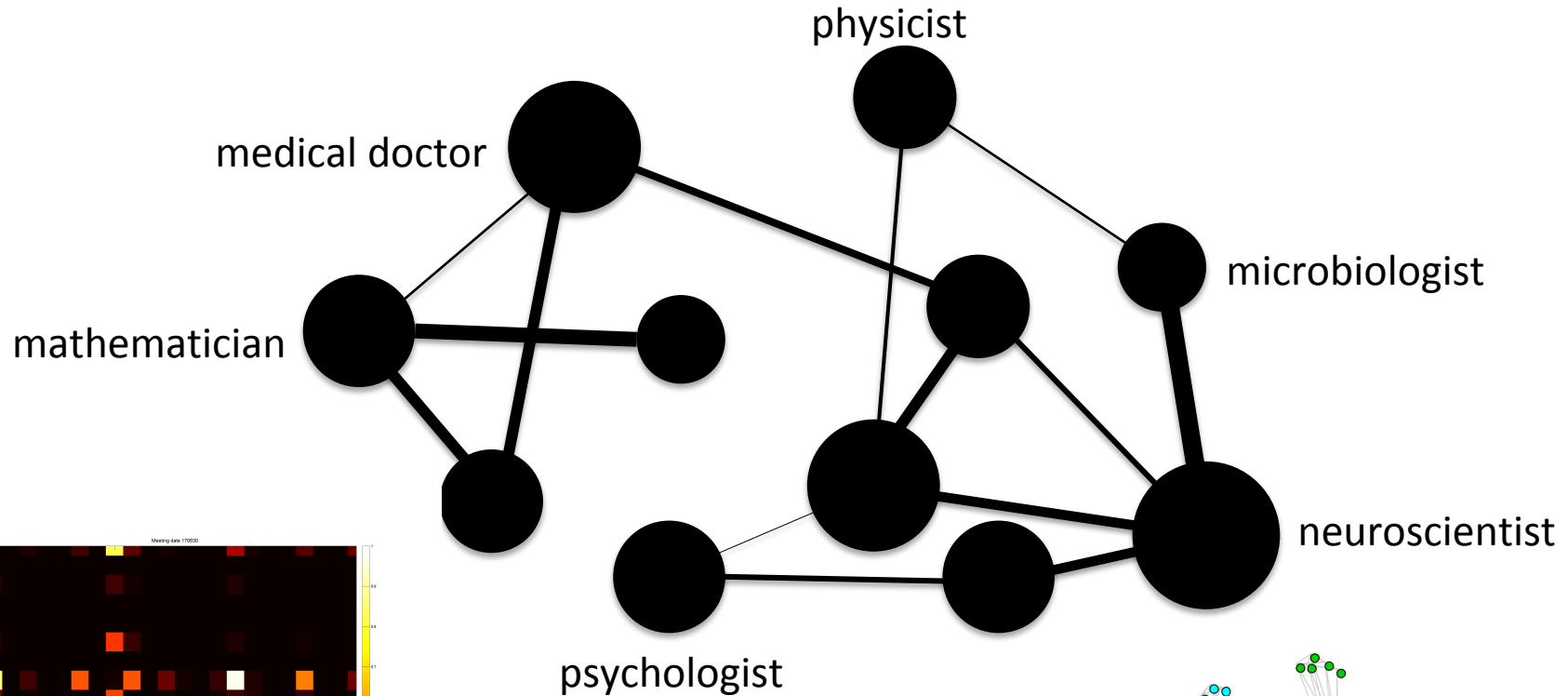
1 | glioma patients undergo tumor resection and postmortem section, which includes both tumor tissue and peritumor/healthy tissue

credit: <https://www.biomax.us/tissue-arrays/Brain/GL806>

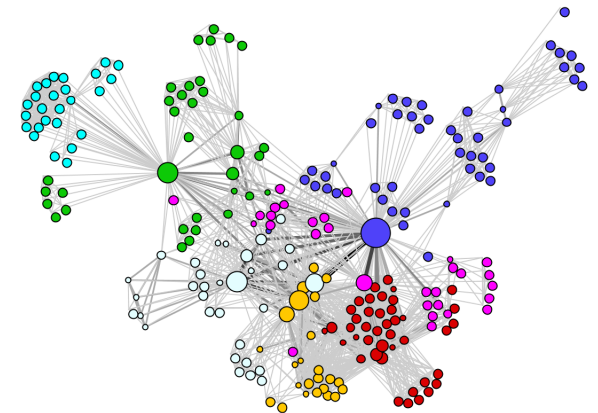


credit: Linda Douw

unexpected yield part 1 | establishing a translational, multidisciplinary team

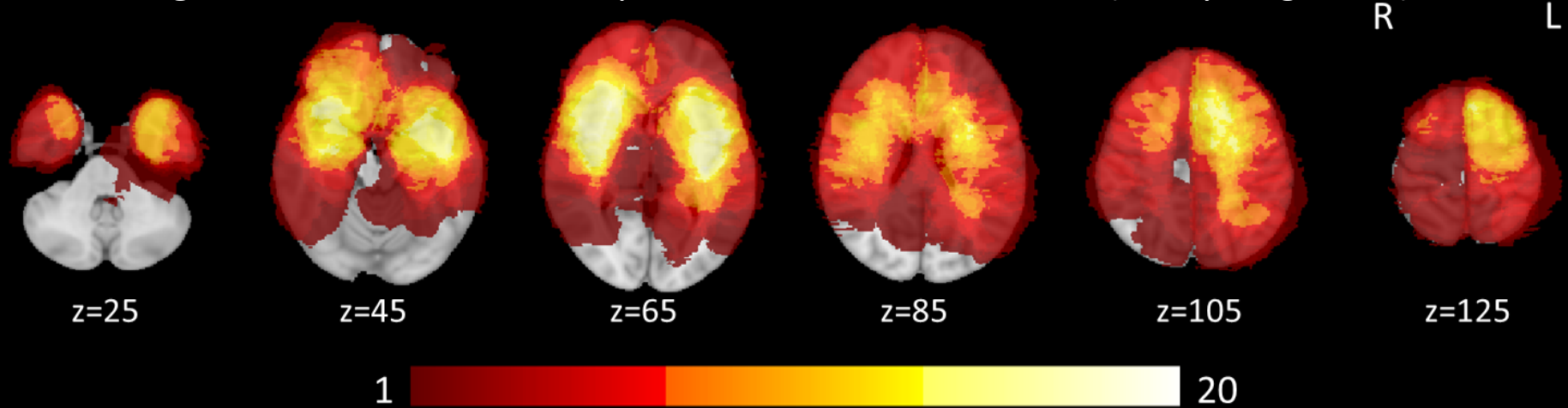


“meetomes”

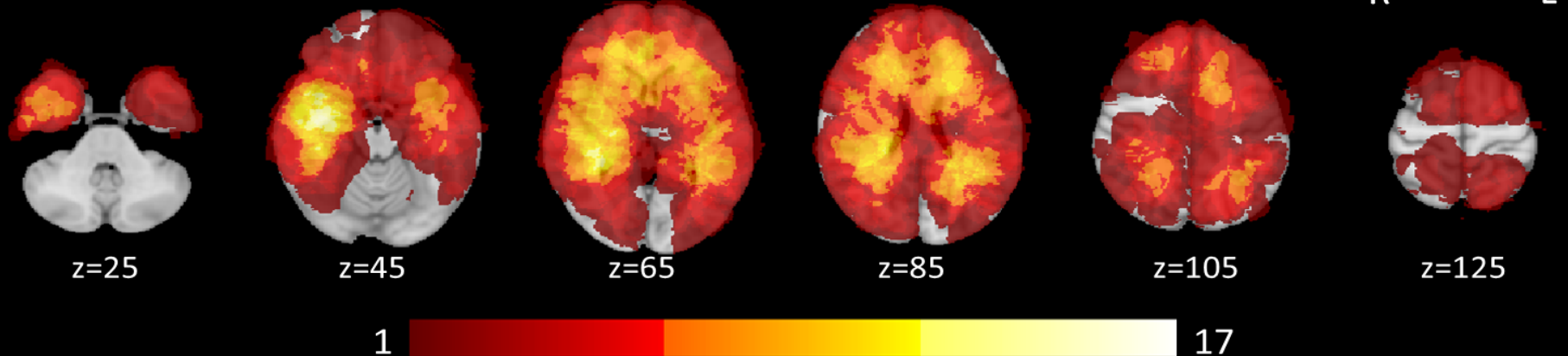


glioma does not occur randomly

glioma occurrence heatmap in Amsterdam cohort n=83 (newly diagnosed)



glioma occurrence heatmap in Boston cohort n=120 (newly diagnosed)

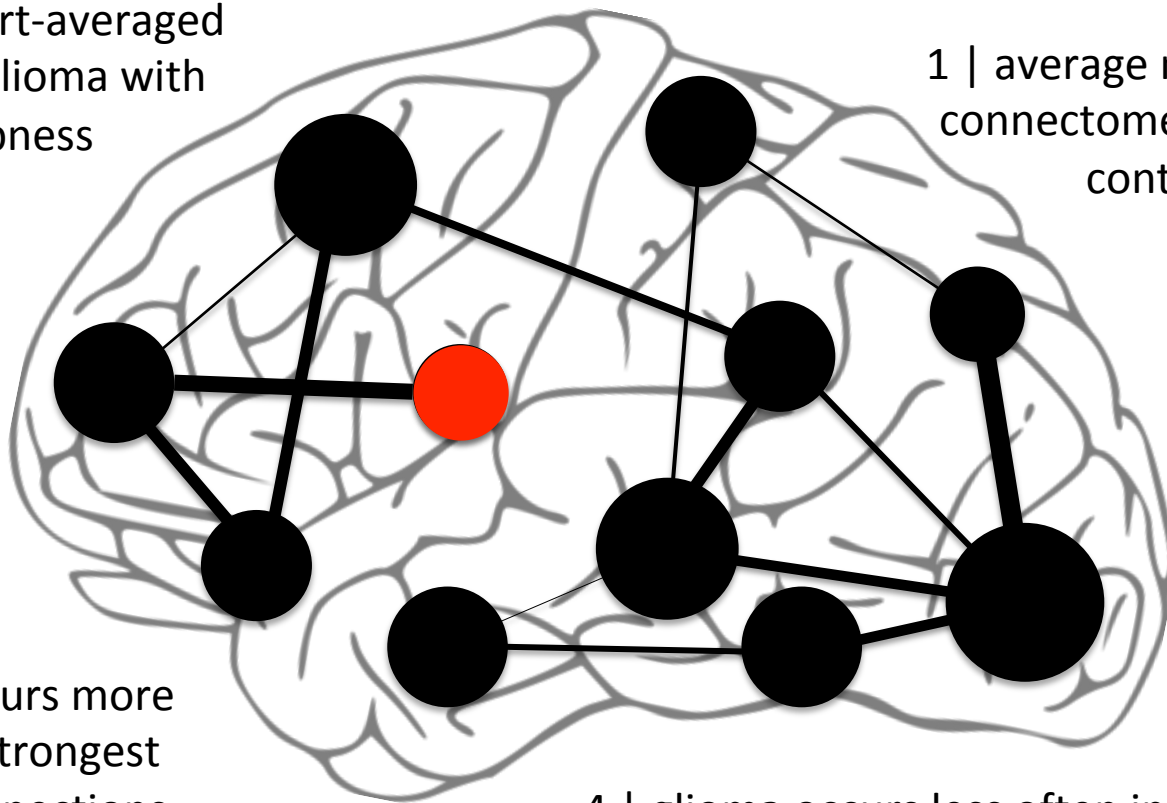


numan et al (under review)

does general occurrence of glioma relate to hubness?

2 | overlay cohort-averaged
occurrence of glioma with
nodal hubness

1 | average macroscopic
connectome of healthy
controls



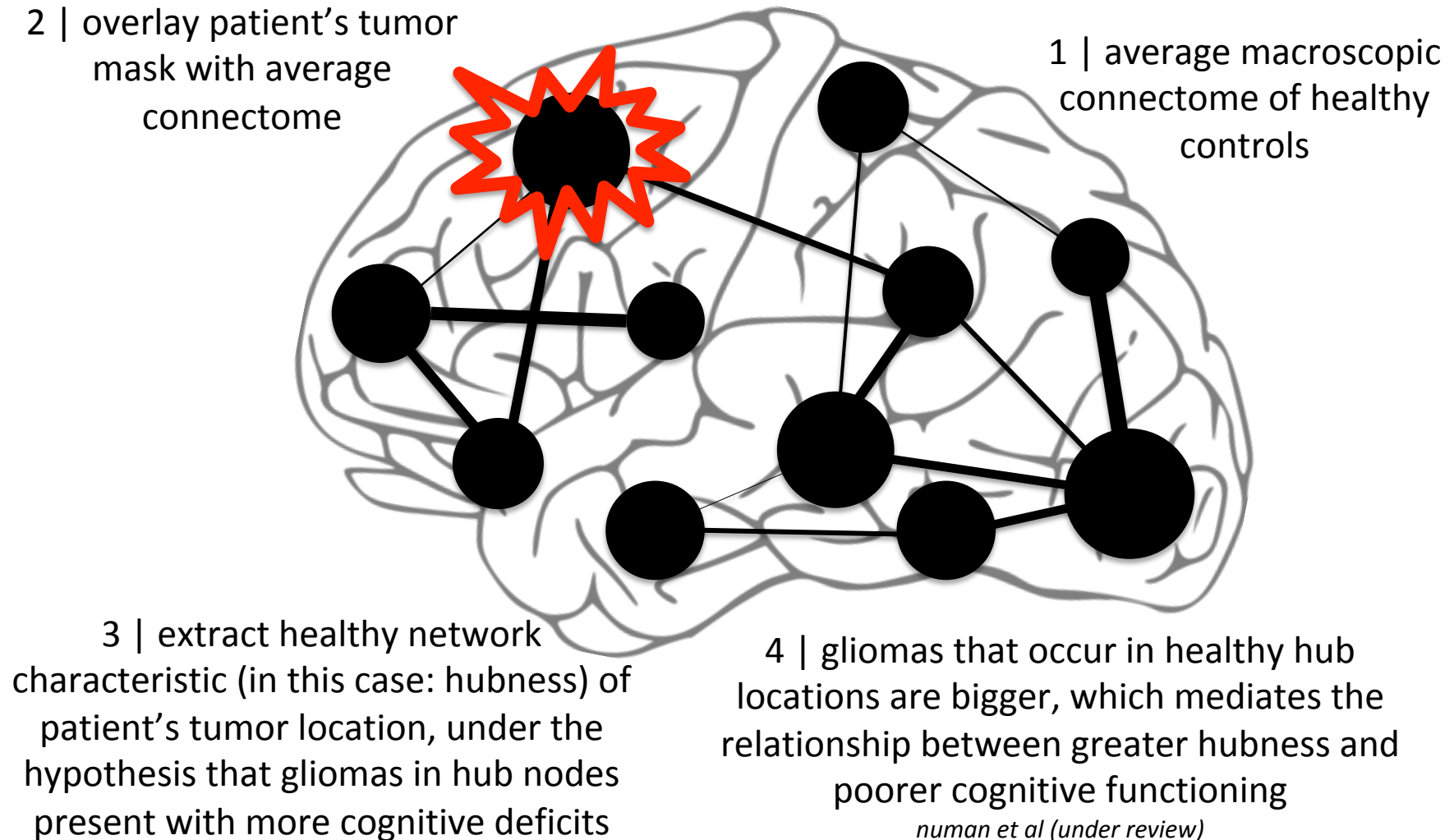
3 | glioma occurs more
often in the strongest
structural connections

numan et al (under review)

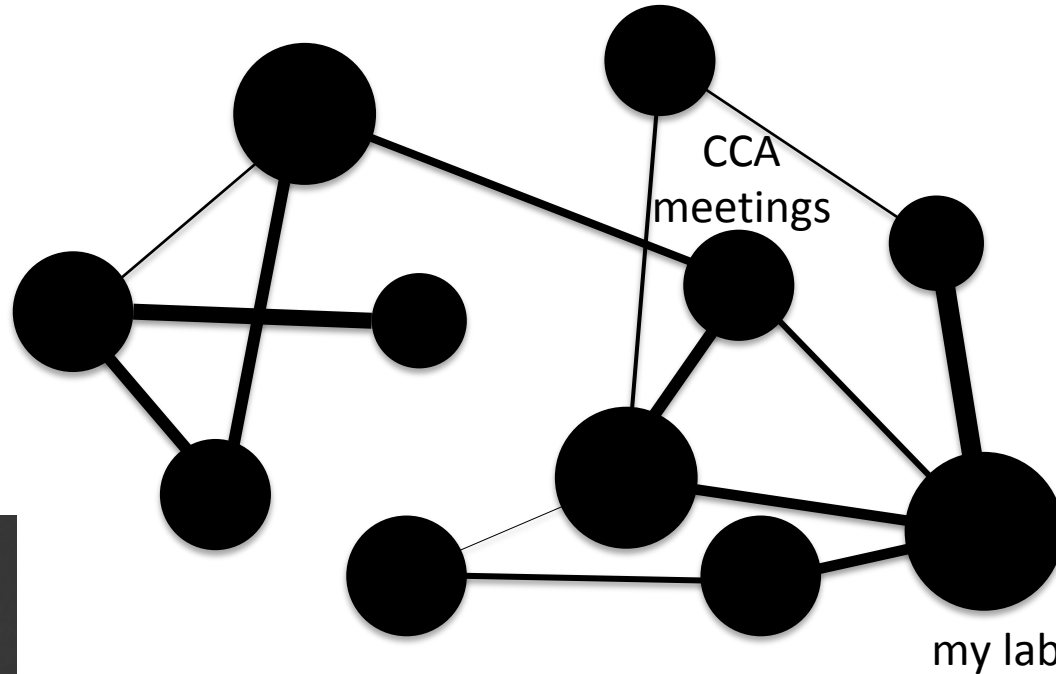
4 | glioma occurs less often in functional
hubs, while there was association between
glioma occurrence and structural hubs

numan et al (under review)

does individual glioma location in the connectome relate to cognition?



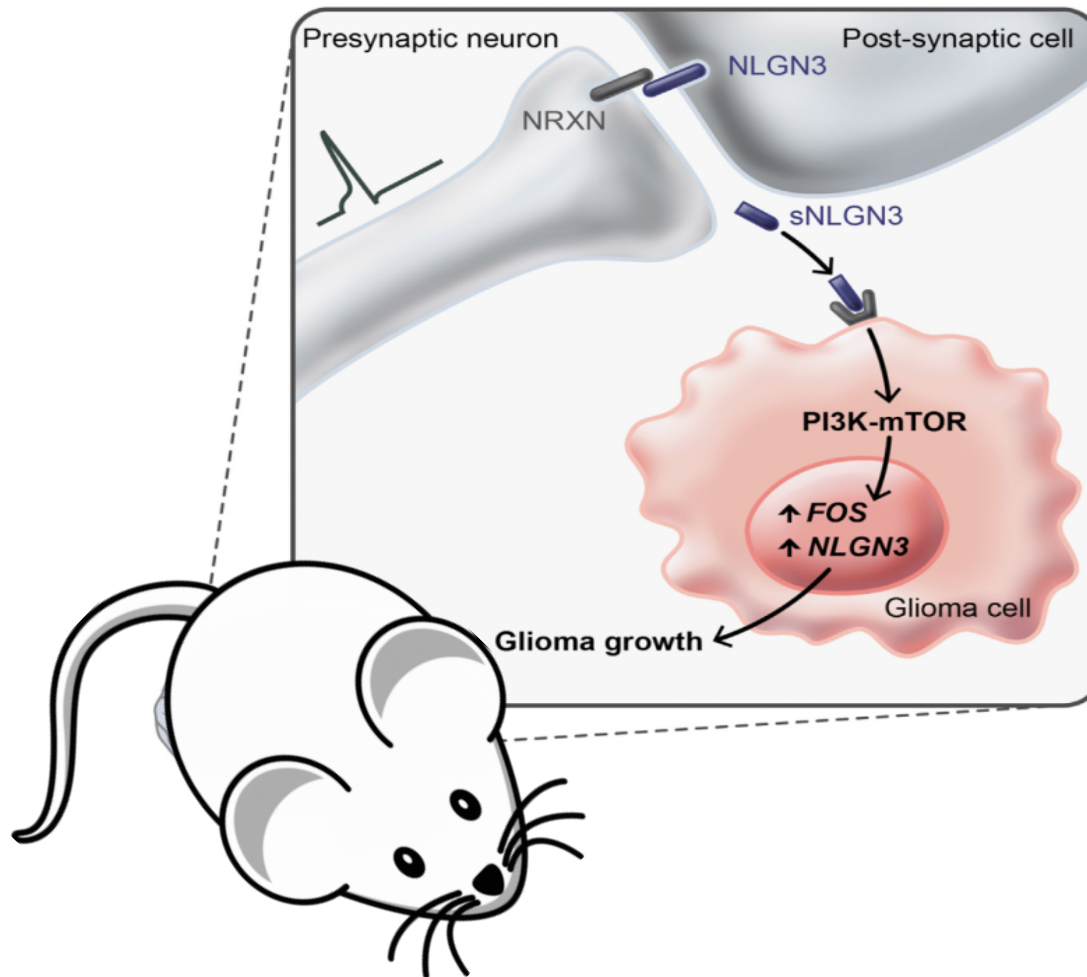
unexpected yield part 2 | openness to inspiration is key



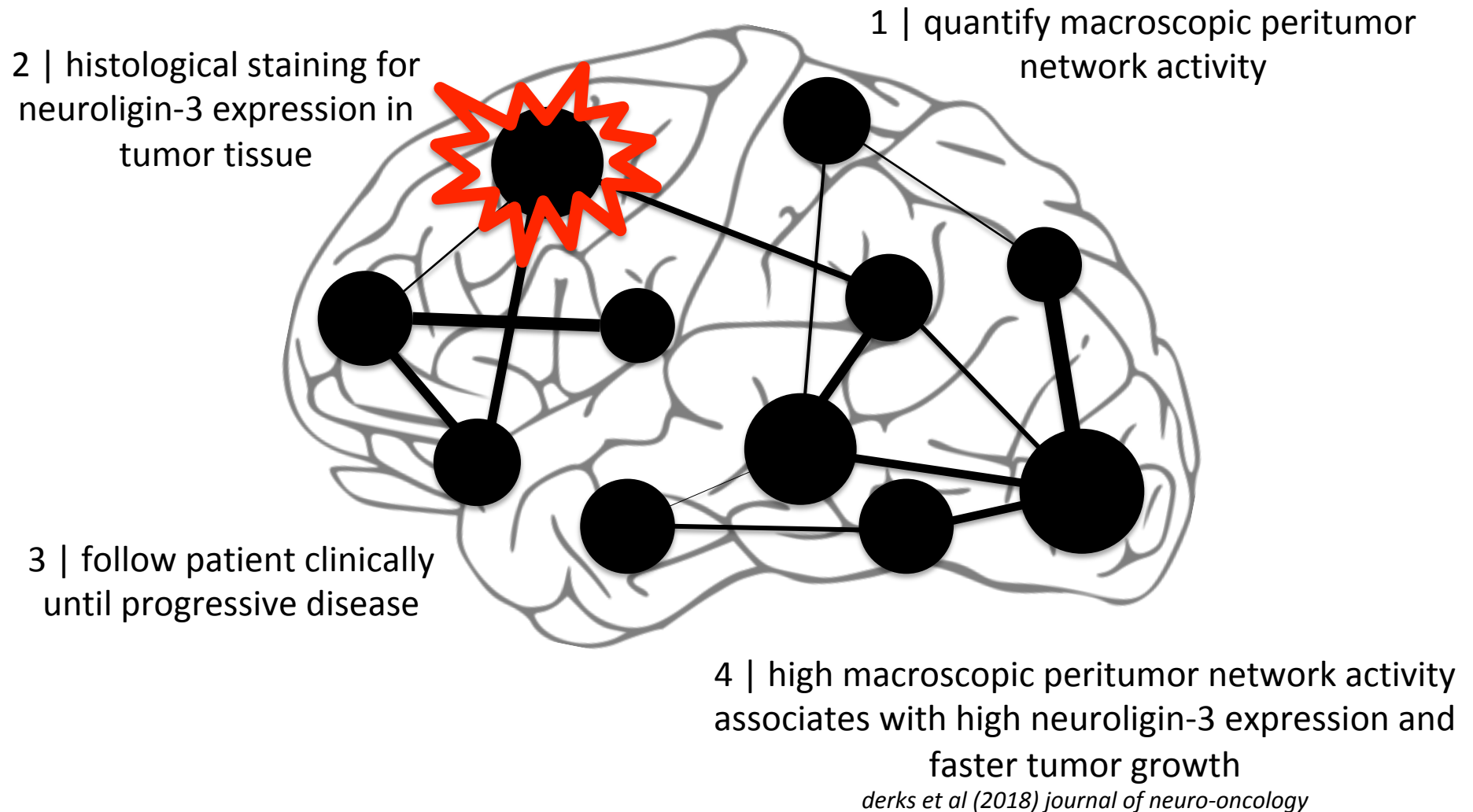
Jolanda
Derks

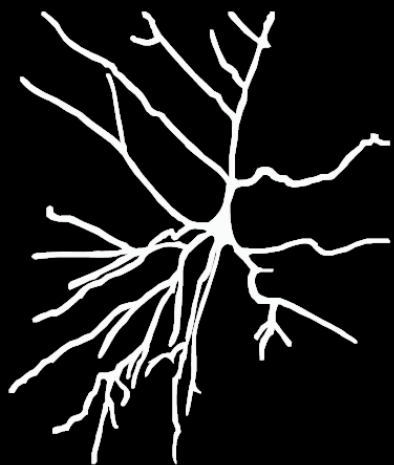


neuronal activity promotes glioma growth through neuroligin-3 secretion and directly

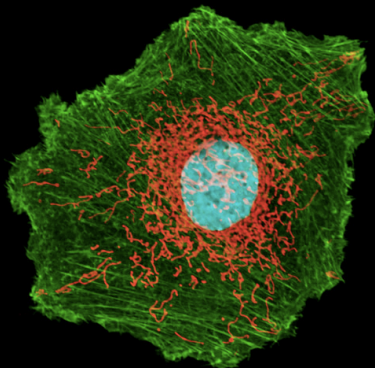
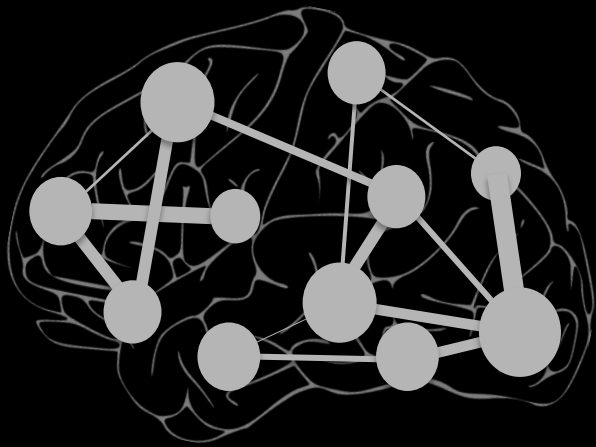


is there synergy between glioma cells, their growth pattern and the connectome?



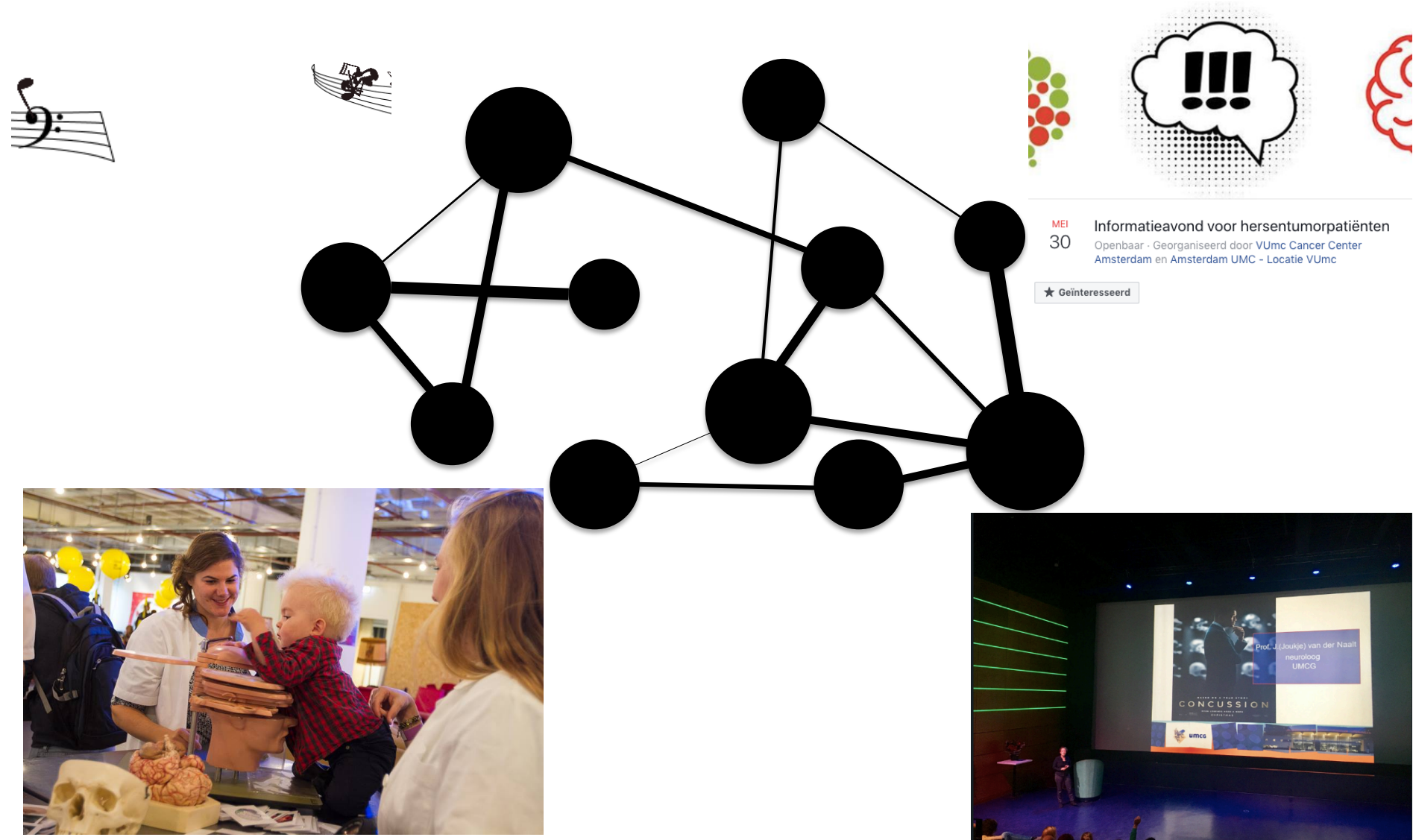


\approx



unexpected yield part 3 |

scientists \approx children \approx people \approx patients



**all patients participating
in scientific research**

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Noam Peled
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Daniel Cagney

University of Heidelberg

Frank Winkler

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