

# Imaging Brain Iron with Quantitative Susceptibility Mapping (QSM)

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# Outline



- Why study iron in the brain
- How can QSM help us with studying iron in the brain
- Current workflow  $\Rightarrow$  Custom end-to-end pipeline

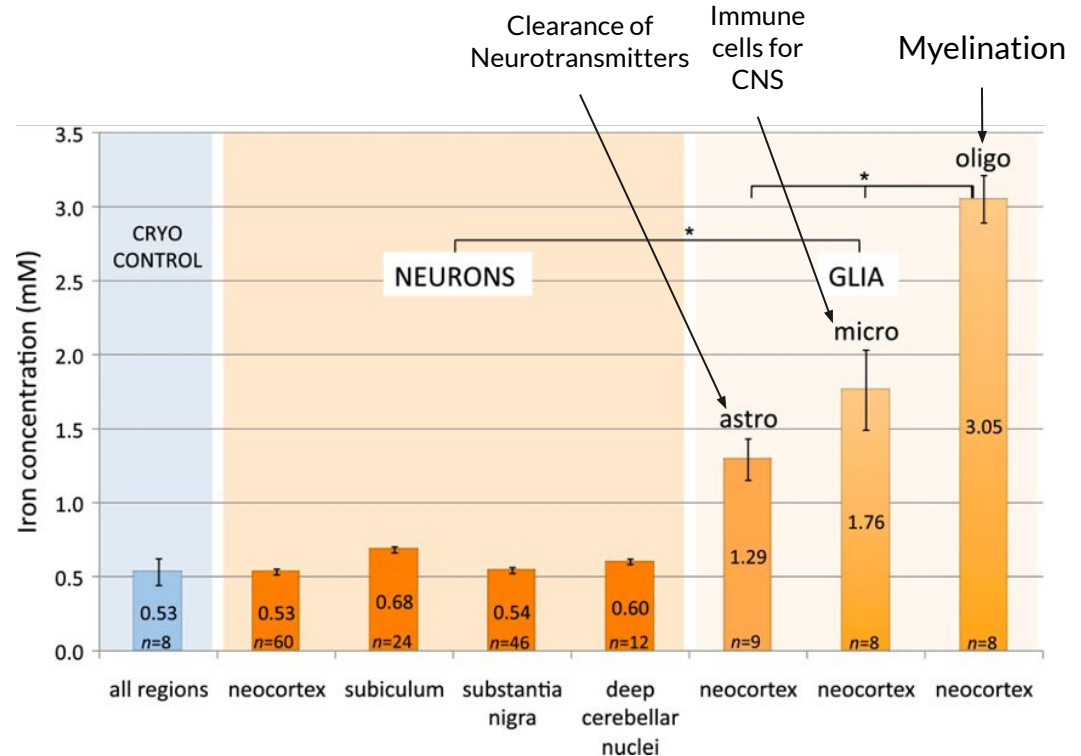


What is brain iron?

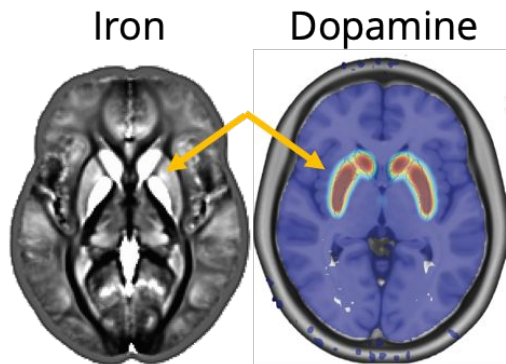
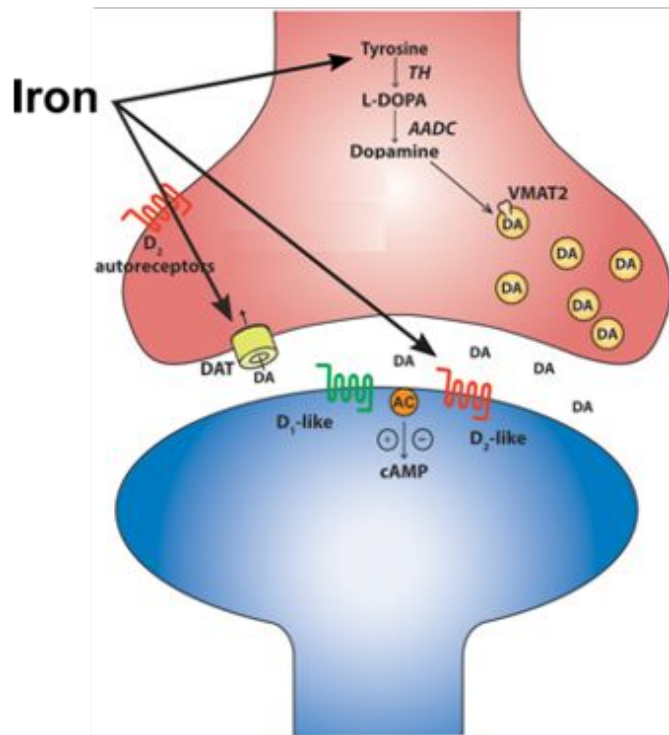
# Iron is important for numerous processes in brain

Iron is an essential co-factor for a number of biochemical and enzymatic reactions that are critical to brain function.

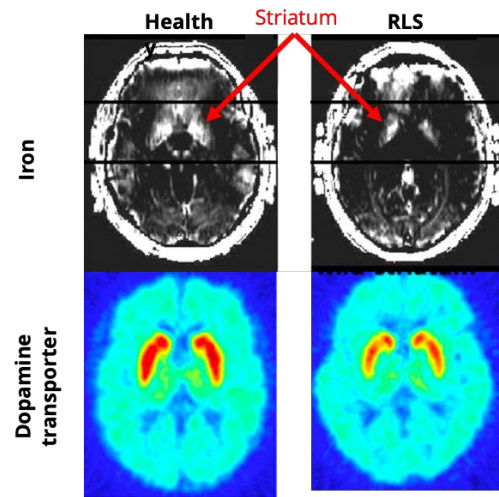
- Neurotransmitter synthesis
- Myelination
- Metabolism



# Iron is tied to dopaminergic system in both physiological and pathological cases



Larsen & Luna, *Dev. Cogn. Neurosci.* 2015  
 Larsen et al., *Nature Communications* 2020  
 Larsen et al., *Journal of Neuroscience* 2020



Haba-Rubio et al., 2005  
 Earley et al., 2011

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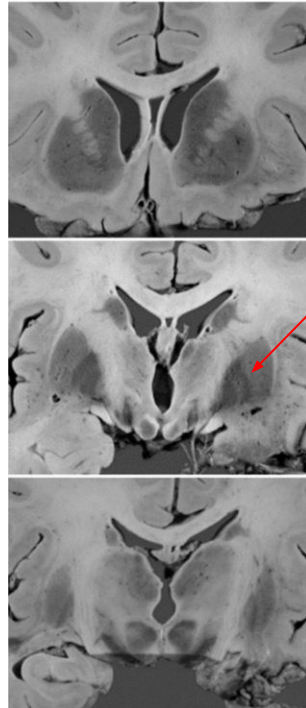


How can we measure iron  
with MRI?

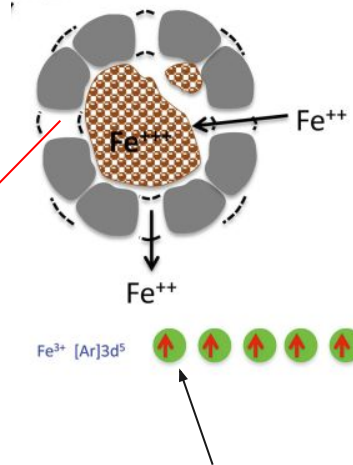
# Iron is paramagnetic

Perls' iron stain

Optical density



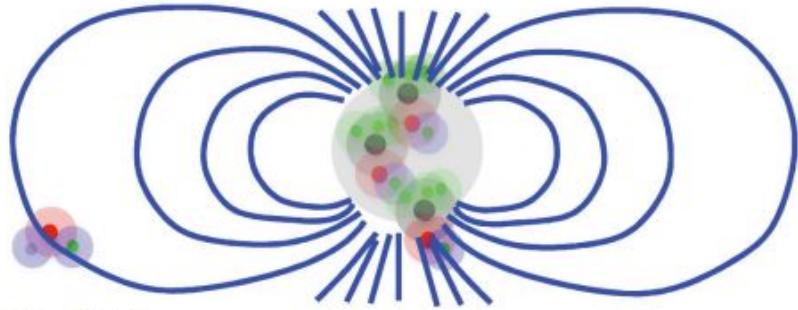
Ferritin  $\Rightarrow$  Paramagnetic



Unpaired electrons of  $\text{Fe}^{3+}$  within  
Ferritin  $\Rightarrow$  strong paramagnetism



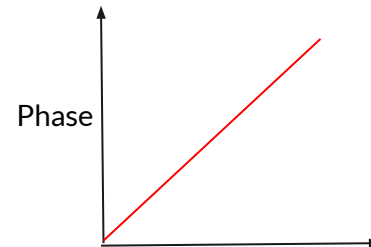
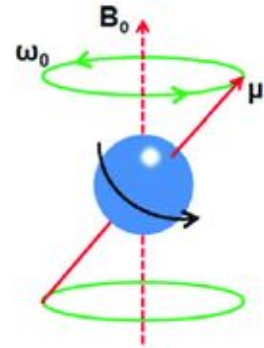
# Tissue magnetization generates its own magnetic field affecting MRI signal



Susceptibility field for  
proton outside the molecule

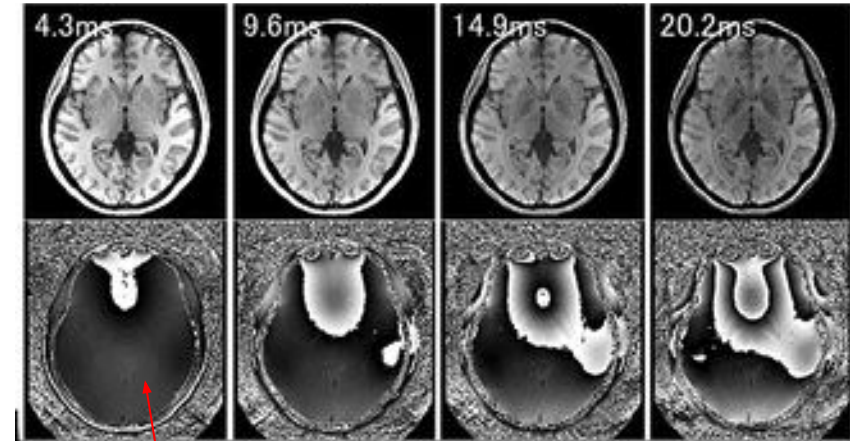
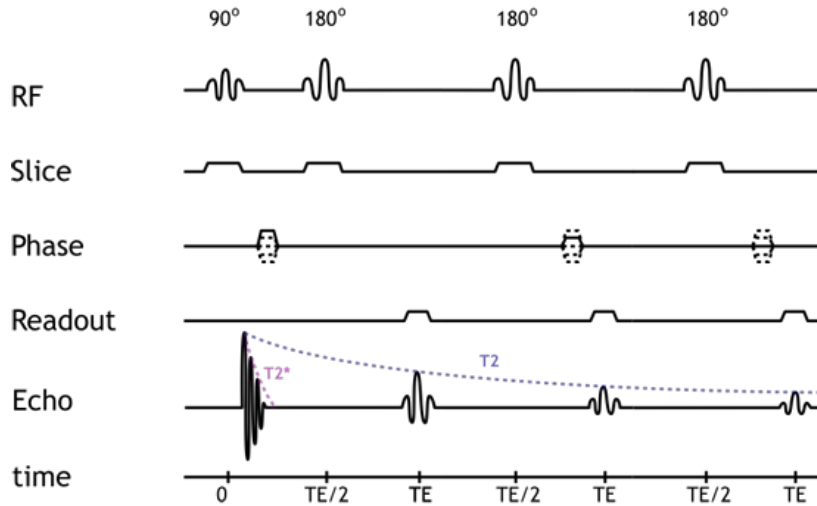
Magnetic shielding for  
proton inside the molecule

Wang and Liu, *Magn Reson Med*. 2015



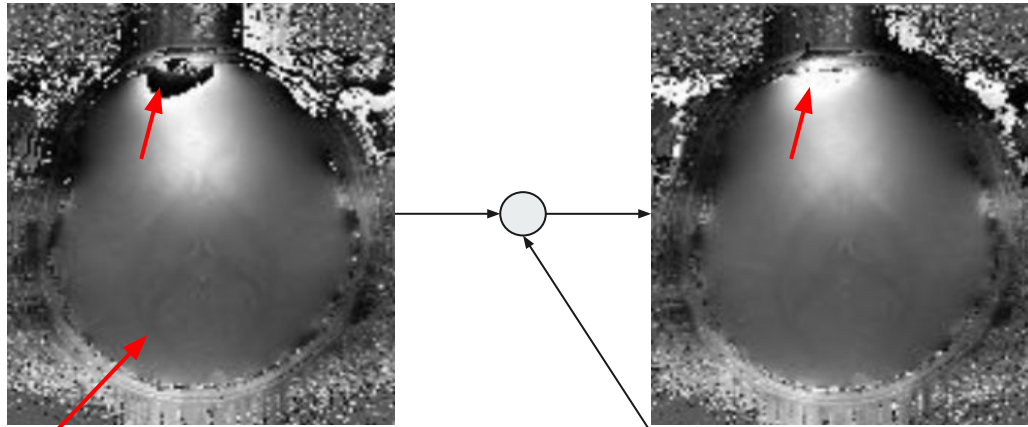
Paramagnetism  $\longrightarrow$  Field Strength

# Quantitative Susceptibility Mapping (QSM) starts with estimation of total field from MRI phase image

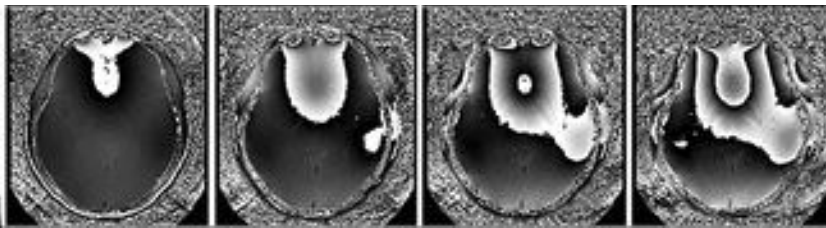


Phase

# Total Field Phase Image has jumps and needs to be unwrapped

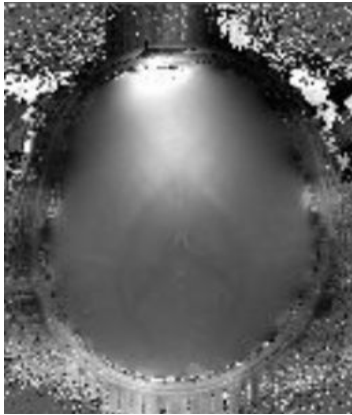
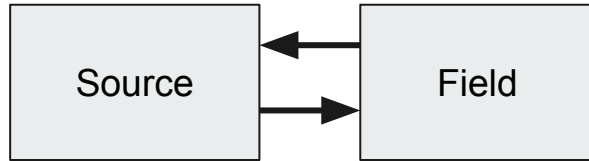


Unwrap Phase Image  
(The estimation was periodic  $\Rightarrow [-\pi, \pi)$ )

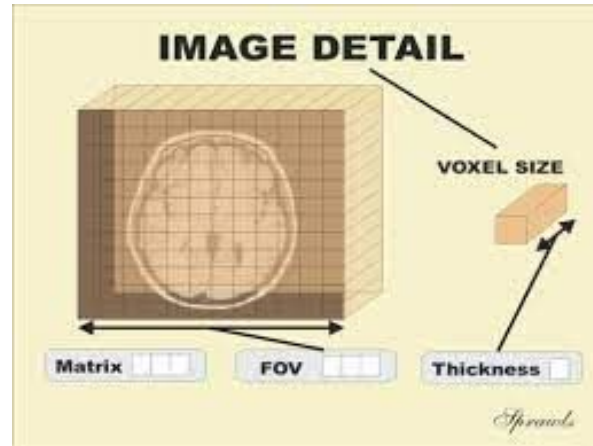


# We have total field, but there are challenges for QSM

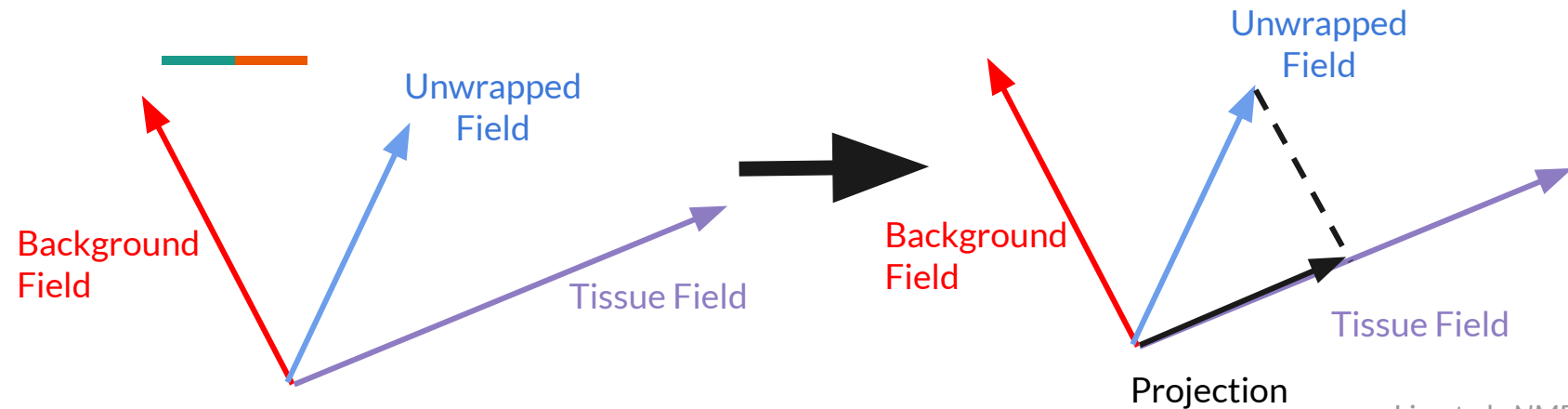
Challenge #1: Excessive number of sources



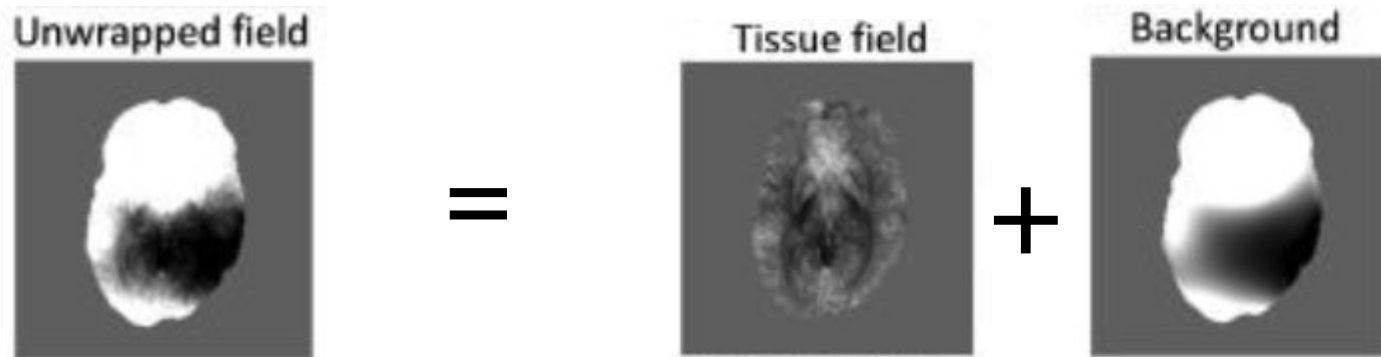
# sources > # detectors



# Solution #1: Background Field Removal

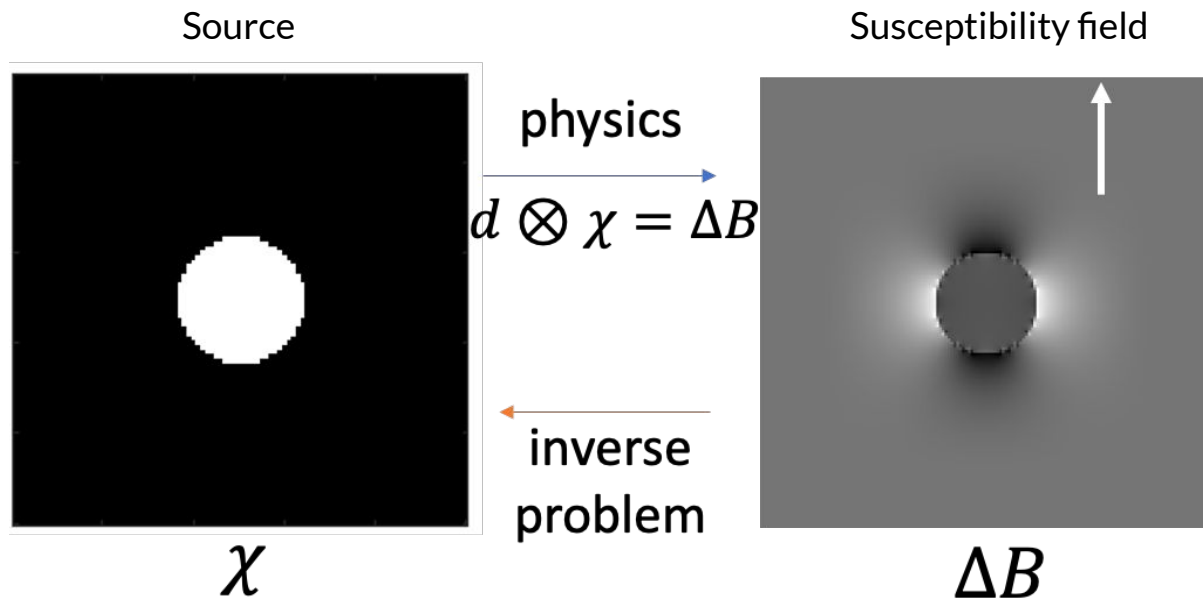


Liu et al., *NMR Biomed.* 2011



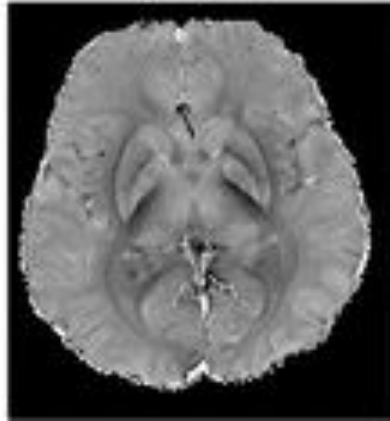
# We now have tissue field, but still have another challenge

## Challenge #2: Field-to-Susceptibility Inversion

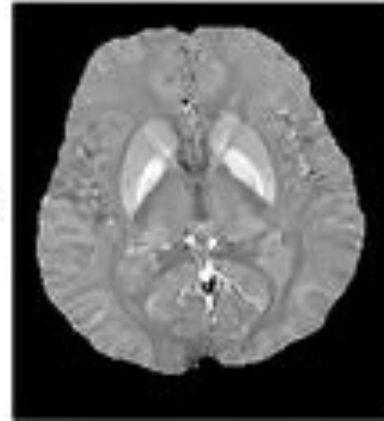


# Dipole Inversion is needed to get the susceptibility mapping

local magnetic field



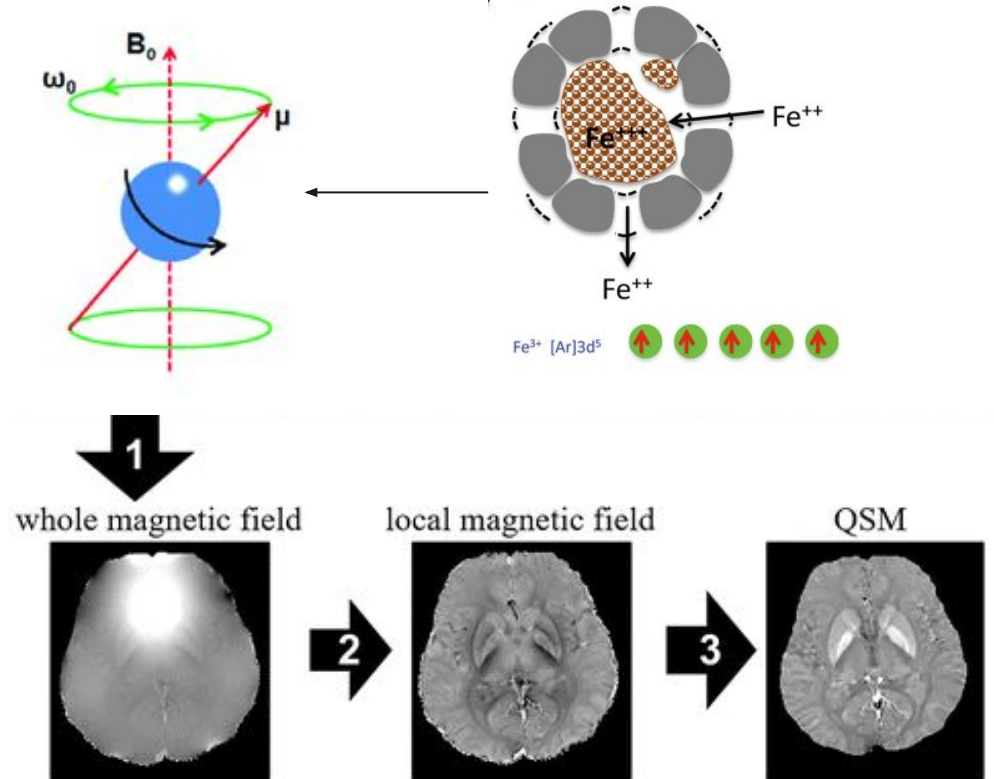
QSM



*"Morphology Enabled Dipole Inversion"*

# Summary for QSM section

- Ferritin stores iron
- External magnetic field changes how the water spin
- QSM measures susceptibility through MRI signal phase
- QSM overcome challenges
  - Background Field Removal
  - Dipole Inversion






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That is great, but what have  
you done so far though?

# Pipeline

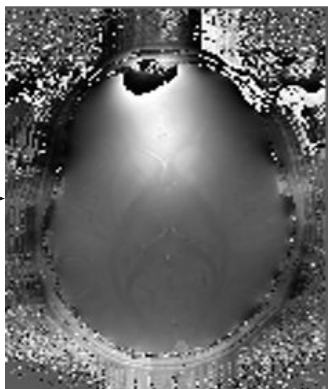


Raw Phase Image



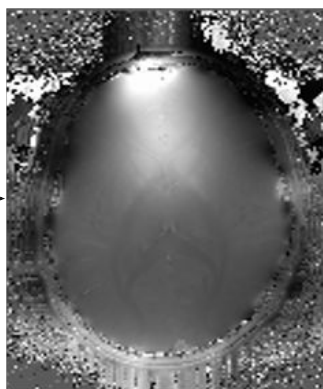
Estimate  
Frequency  
Offset

Wrapped Phase Image



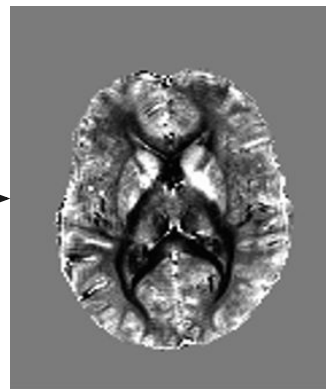
Phase  
Unwrapping

Unwrapped Phase Image



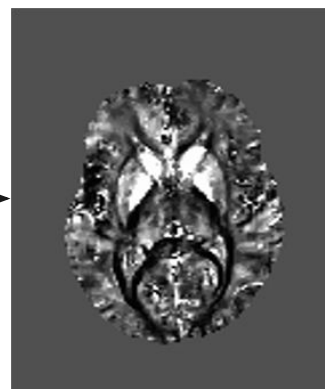
Background  
Field  
Removal

Tissue Field Image



Dipole  
Inversion

Susceptibility Map





# Dataset

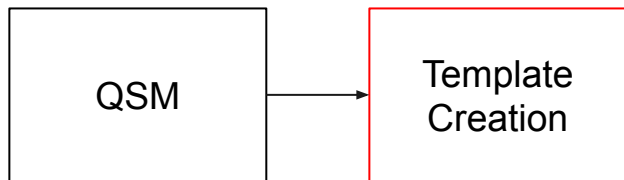
## EF

- ~175 subjects
- 3 timepoints
- Age: 8-19
- Psychosis Spectrum
- ADHD
- Typically Developing

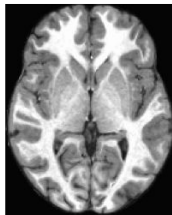
## MOTIVE

- ~154 subjects
- 2 timepoints
- Age: 16-28
- Psychosis Spectrum
- Typically Developing

# Pipeline



Subject 1

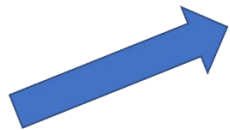
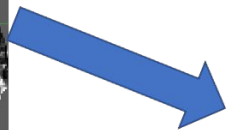
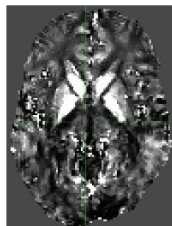
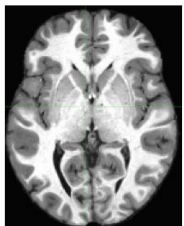


T1w Image



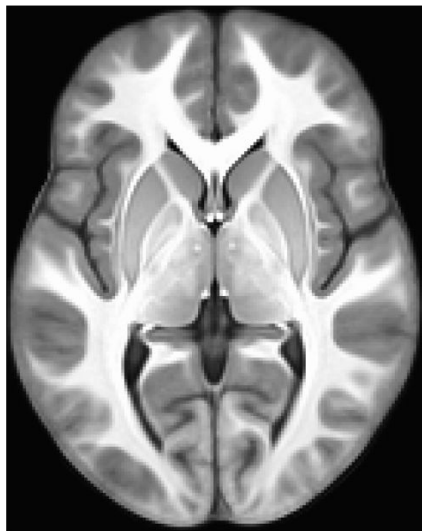
QSM Output

Subject  $n$



`antsMultivariateTemplateConstruction2`

T1w Template



QSM  
Template

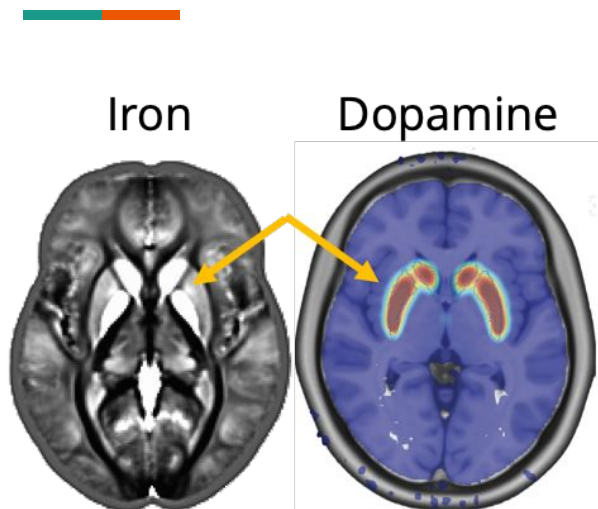




## Future Directions

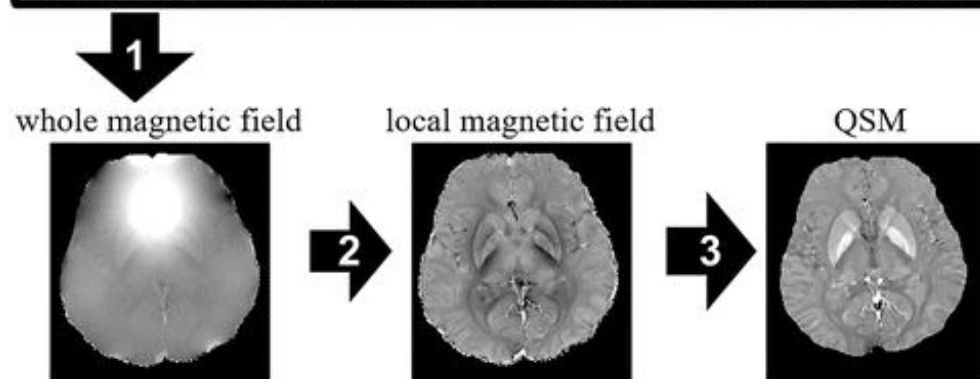
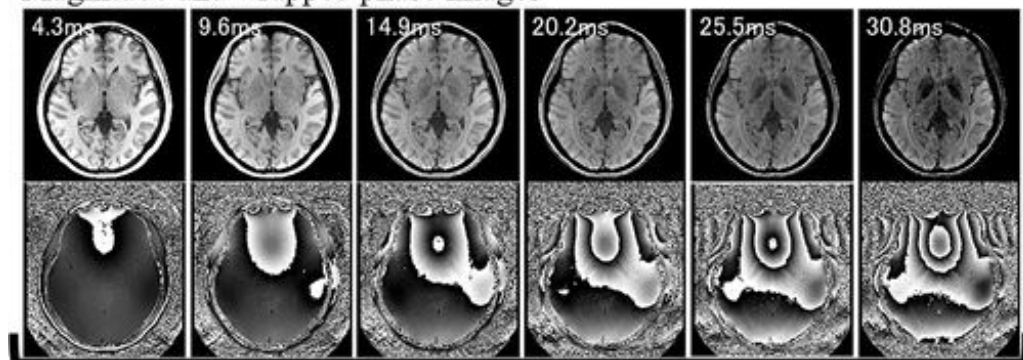
- Differences in QSM level between Psychosis and TD youths
- Reproducible pipeline for other studies

# Summary



Larsen & Luna, *Dev. Cogn. Neurosci.* 2015  
Larsen et al., *Nature Communications* 2020  
Larsen et al., *Journal of Neuroscience* 2020

Magnitude and wrapped phase images





# Acknowledgements

- Bart Larsen
- Theodore Satterthwaite
- Daniel Wolf
- David Roalf
- Walter Witschey
- Alexandra Roberts (Cornell)
- Kahini Mehta
- Chloe Savage
- Matt Cieslak





Thank you!!