COLUMBIA UNIVERSITY MEDICAL CENTER

M²OVE AD

SUNY DOWNSTATE MEDICAL CENTER

Interdisciplinary Research to Understand the Interplay of Diabetes, Cerebrovascular disease and Alzheimer's Disease (DiCAD; RF1AG051556)

Adam Brickman, PhD (CUMC)

José A. Luchsinger, MD, MPH (CUMC)

Herman Moreno, MD, PhD (SUNY Downstate)

Overarching hypothesis and approach

- HYPOTHESIS:

Hyperglycemia causes both CVD and AD which interact and mediate the association with cognitive impairment

- APPROACH:

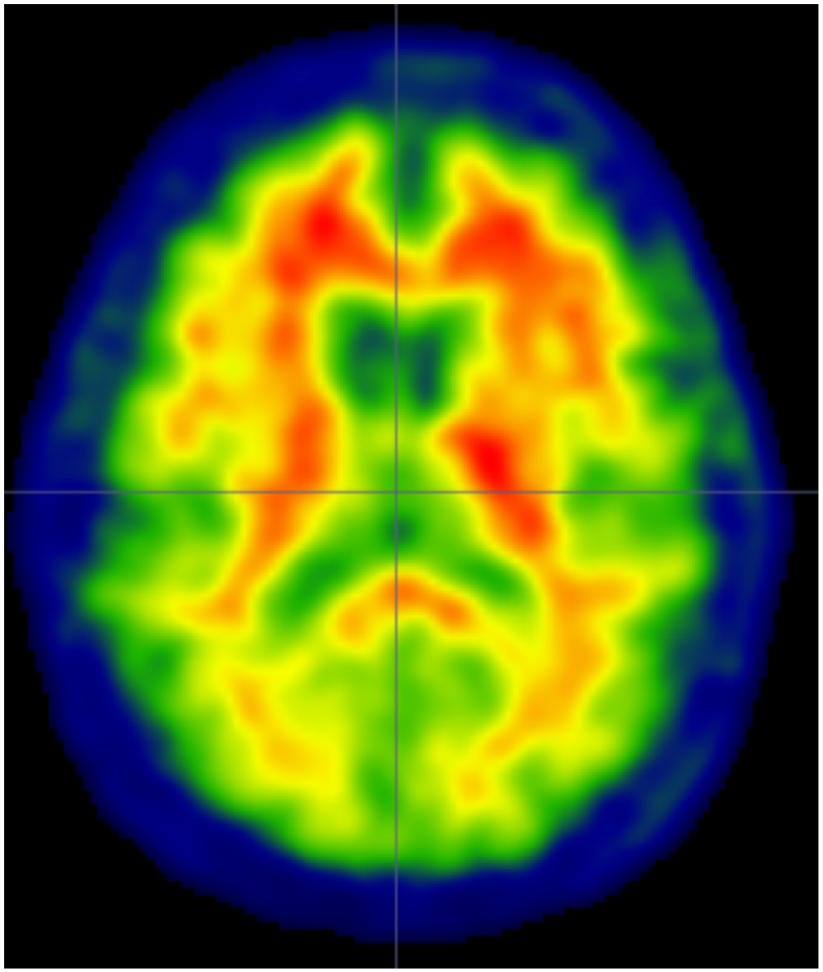
To conduct complementary human and mice studies to understand mechanisms

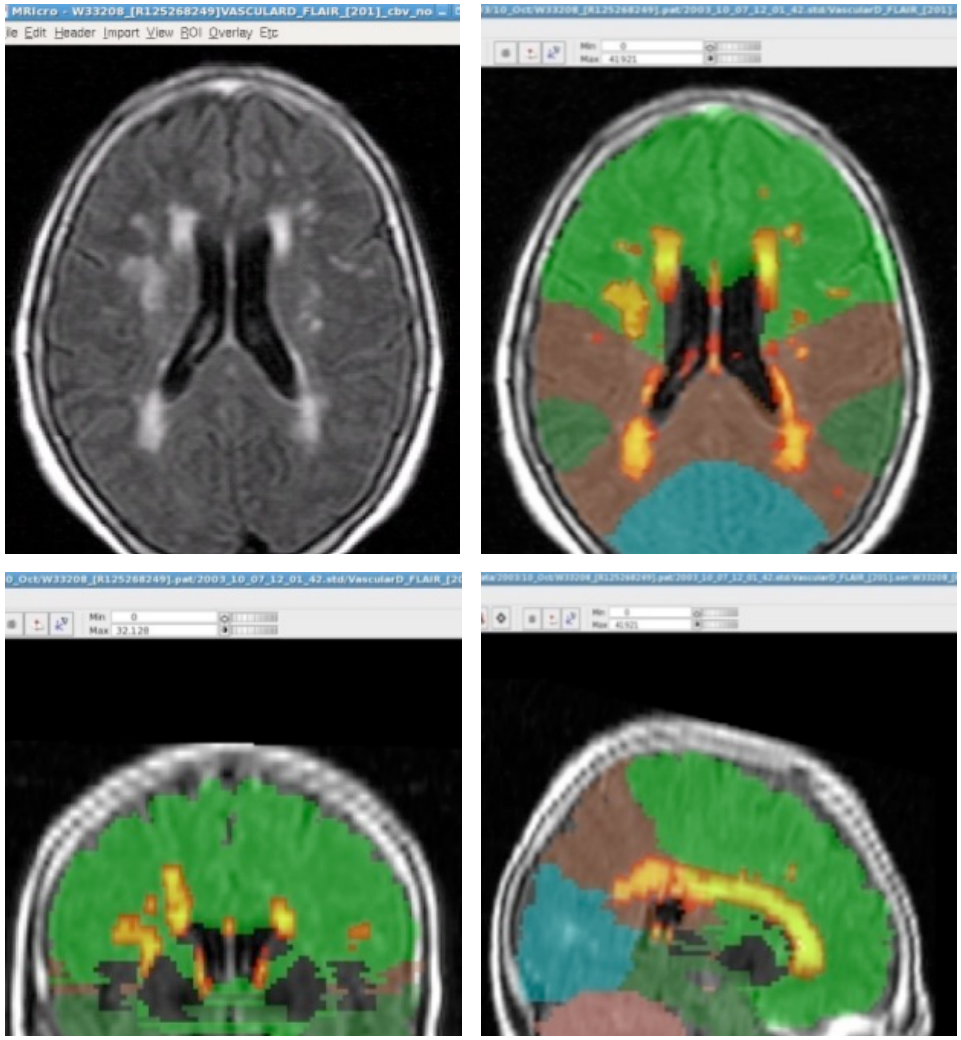
Primary aim. *To examine the association of diabetes with the interplay of AD and CVD in humans and mice*.

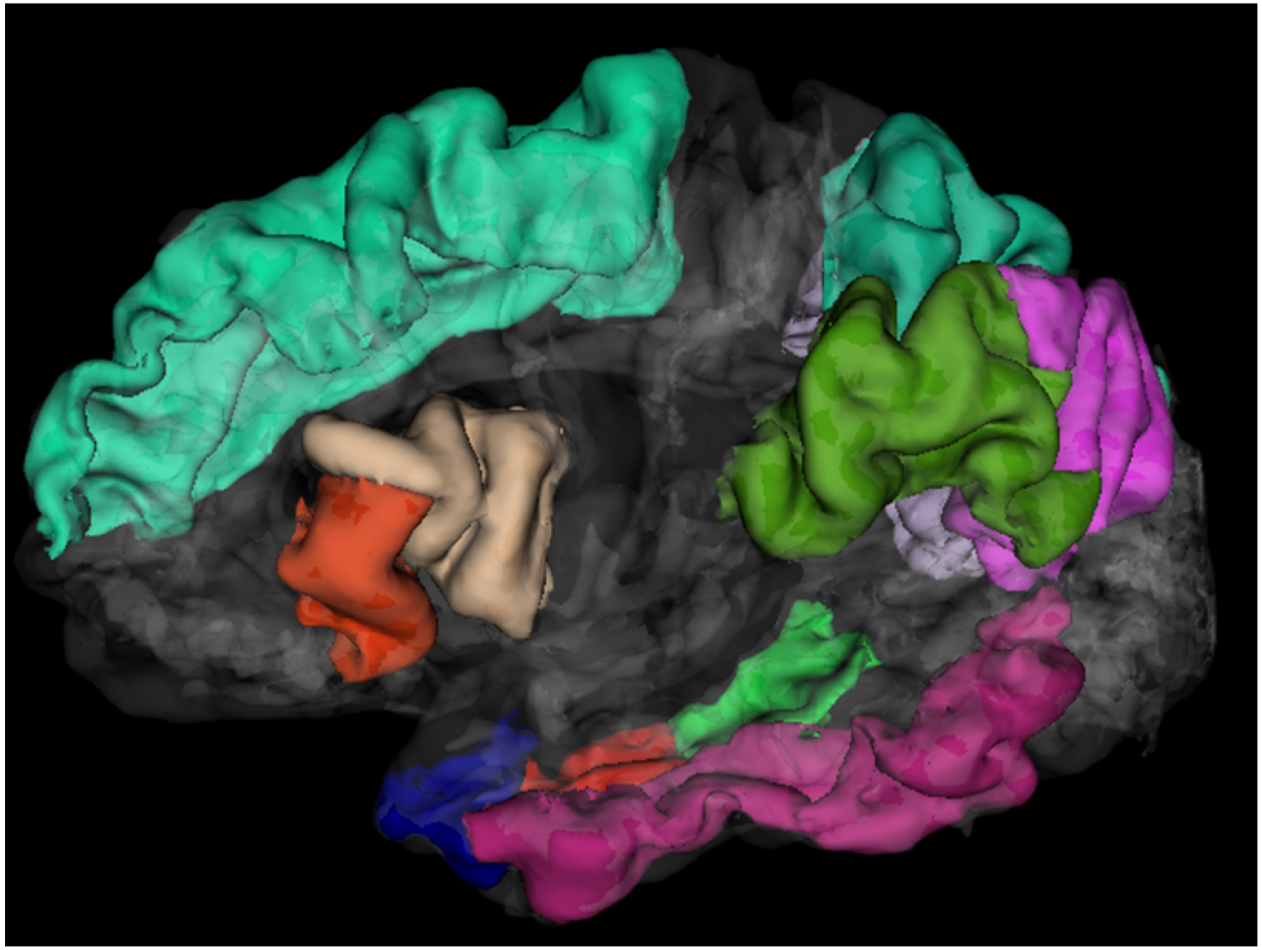
• Humans		• Mice
• Cohort study of 200 late middle aged adults	→	• Experiments in young and old mice (db/db, db/+, APP/PS1, C57, mixed)
• Metabolic profile: OGTT, HbA1c, insulin, extended panel	→	• Metabolic profile: HbA1c, glucose, insulin, extended panel
• Cognition: with NS battery	→	• Cognition/behavior: PPA, APA,NOR
• AD pathology: Amyloid and Tau PET	→	• AD pathology: IHC/histology
• Cerebrovascular disease: MRI	→	• Cerebrovascular disease: tMCAo
• Physiology: brain DMN on MRI	→	• Physiology: EP profile EC-HC
• Discovery: Metabolomics, proteomics, genomics		• Metabolomics, proteomics
COLUMBIA UNIVERSITY		**SUNY DOWNSTATE**

Human sample characteristics

Variable	Value
Number of participants	139
Age in years	63.3 ± 4.3
Women	74.8%
Education in years	10.0 ± 3.8
APOE-ε4 %	27.4%
HbA1c in %	6.1 ± 1.4
Normal glucose tolerance %	44.6%
Pre-diabetes % %	30.9%
Undiagnosed diabetes	4.3%
Known diabetes %	22.3%

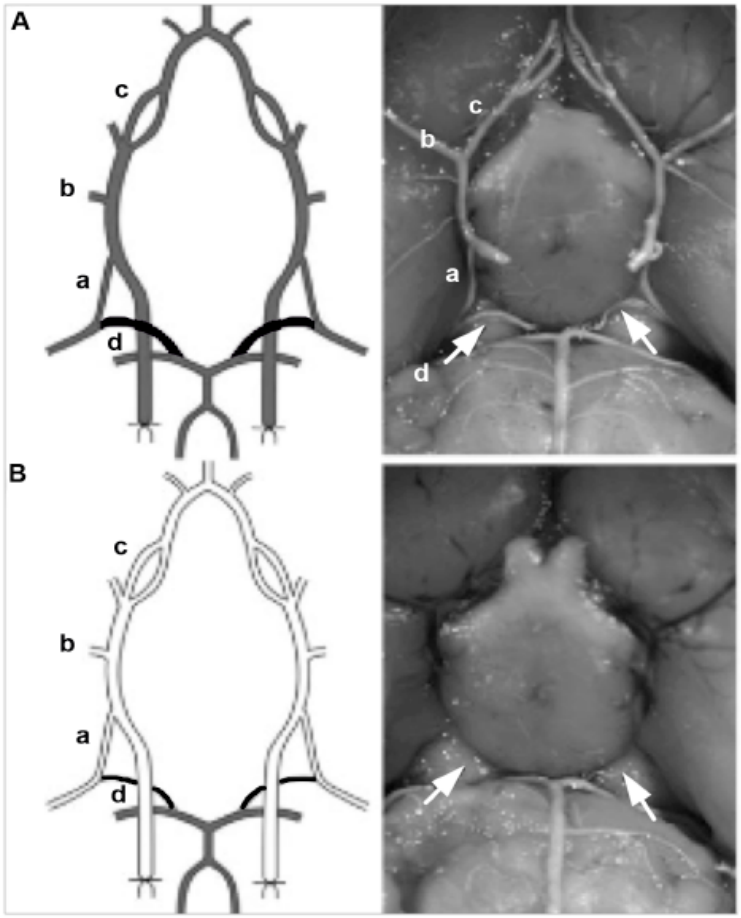


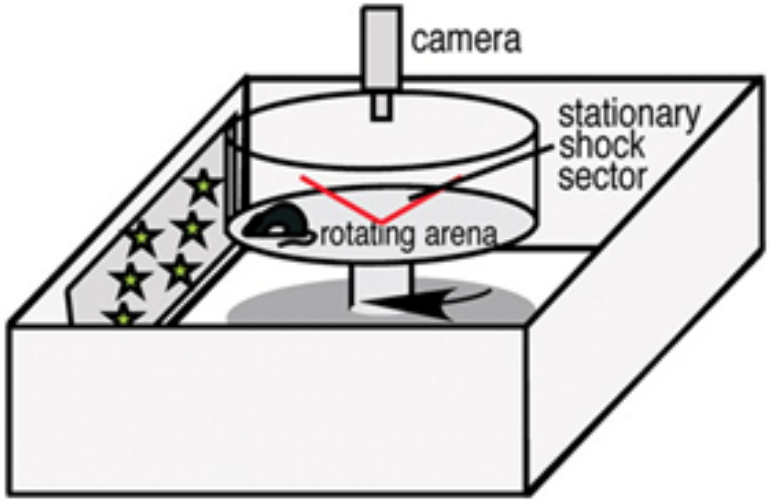

MRIcro - W33208_[R125268249]VASCULARD_FLAIR_[201]_cbv_no
File Edit Header Import View ROI Overlay Etc

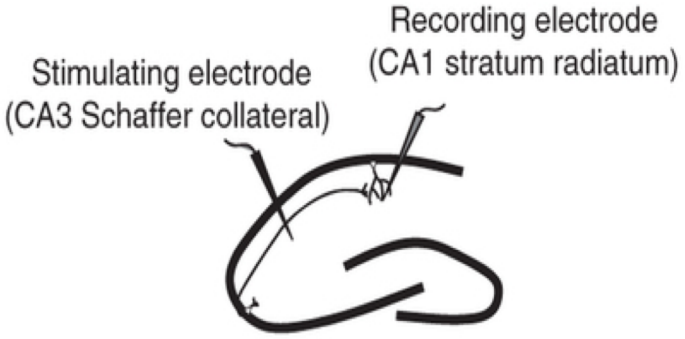


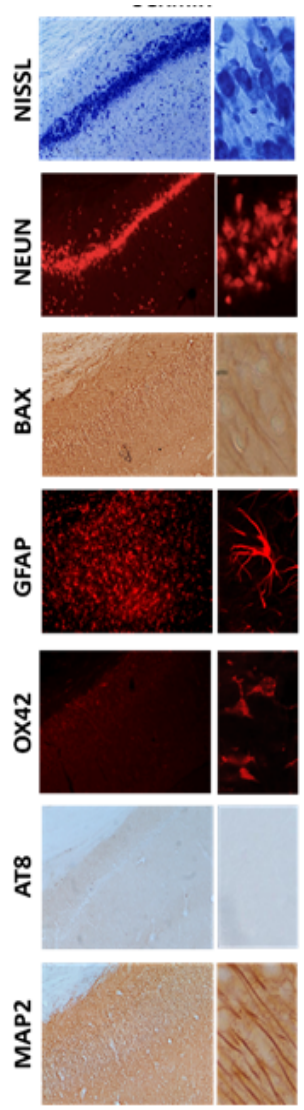
Mouse models

- **Db/Db mice, Db/WT**
- **J20, APP/PS1, C57**
- **Mixed Db APP/PSI**
- **Young and old**
- **With and without stroke**




camera
stationary
shock
sector
rotating arena


Recording electrode
(CA1 stratum radiatum)
Stimulating electrode
(CA3 Schaffer collateral)


NISSL
NEUN
BAX
GFAP
OX42
AT8
MAP2

Future directions

- Conduct metabolomics, lipidomics in human sera and in mouse sera, brain, liver, gut in coordination with the AD metabolomics consortium
- Conduct proteomics and genomics in collaboration wiht M^2OVE-AD AND AMP-AD partners
- Examining insulin resistance and adipokines

Data sharing

- All data uploaded in Synapse
- Biospecimen repository

Conclusions

- Hyperglycemia seems to increase vascular disease and neurodegeneration but its relation with amyloid burden needs further exploration
  - Examination of tau pending
- Sex is an important modifier that needs to be examined
- AD and neurodegeneration have important metabolic signatures that require further study

Acknowledgements

- Duke University
  - Rima Kaddurah-Daouk
- Rush University
  - Chris Gaiteri
- Columbia University
  - William Kreisl
  - Qulamreza Razlighi
  - Phil DeJager
- Hebrew Home at Riverdale
  - Jeanne Teresi
- SUNY Downstate
  - Frank Barone
- NIH
  - Suzana Petanceska
- SAGE
  - Lara Mangravite
  - Mette Peters