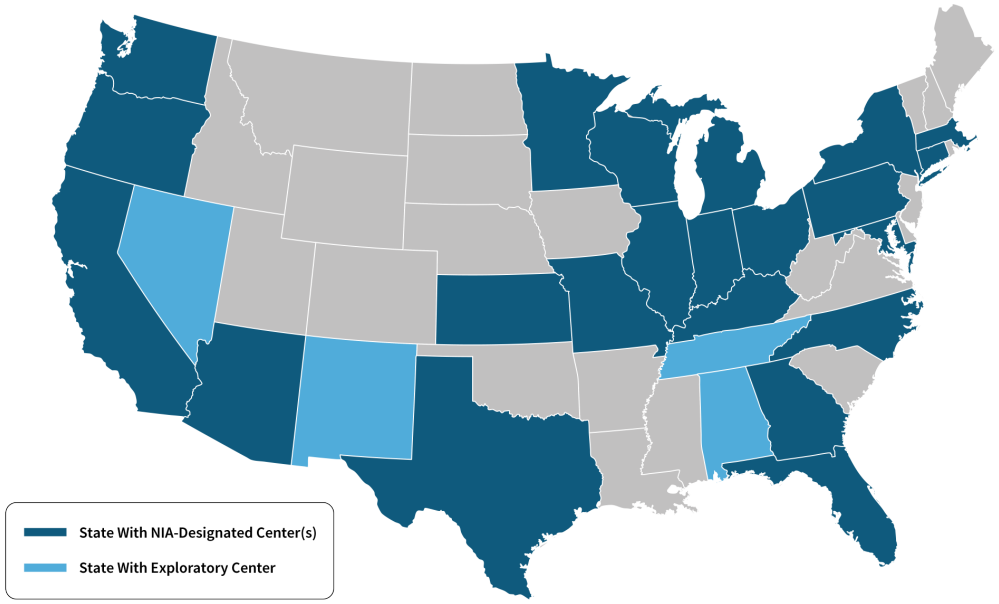
ADRC – NeuroBiobank Working Group to Advance Brain Donation and Utilization for ADRD Research:

Summary of Pilot Program (so far)

National Institute on Aging
DESIGNATED
Alzheimer's Disease Research Center



NeuroBioBank
Facilitating Research and Creating Awareness

NIH Alzheimer's Disease Centers Panel Recommendations (2017)

- Improve autopsy consent processes for research broadly to help achieve diversity
- Maximize post-mortem rates
- Prioritize clinically well-characterized research participants and those of particular interest
- Expand opportunities for autopsies beyond UDS and clinical core participants when they facilitate AD and ADRD research
- Establish transparent guidelines for acceptance, retention, and sharing of tissue and data for research purposes to eliminate barriers and facilitate broad access to samples for research.
- Augment approaches to increase autopsy material from cognitively normal individuals

NAPA ADVISORY COUNCIL ON ALZHEIMER'S RESEARCH, CARE, AND SERVICES
Research Subcommittee: Recommendation 5

Federal agencies should develop a strategy and infrastructure to increase ethical and open sharing of, access to, and utilization of research data and samples. There should be a continued emphasis on ethics, in collaboration with academia, the pharmaceutical industry, biotech and information system industries. This strategy should accelerate the pace of scientific discovery in AD/ADRD science by addressing a comprehensive range of issues including cross-sector data and biosample sharing practices and policies, data harmonization and interoperability, and the training of data scientists and biobanking experts in AD/ADRD research.

- Special emphasis is needed on data sharing of completed biomarker studies and drug and non-drug clinical trials, including industry-sponsored trials. Patient advocacy and regulatory changes may be required.
- Emphasis is needed on methods for early recognition and progression of disease using cutting edge technologies, and establishment of biobanks of cells and biofluids from well phenotyped, diverse individuals reflective of the heterogeneity of AD/ADRD.
- To expand access to brain tissue needed for AD/ADRD research purposes, NIH should explore gaps in tissue availability for research, and review and refine the current infrastructure at NIH supported tissue repositories, including the NeuroBioBank and Alzheimer's Disease Research Centers (ADRCs), to fill these gaps. Continuing attention should be placed on consent issues, harmonizing protocols, and data sharing practices.

Slide courtesy of Dr. Nina Silverberg

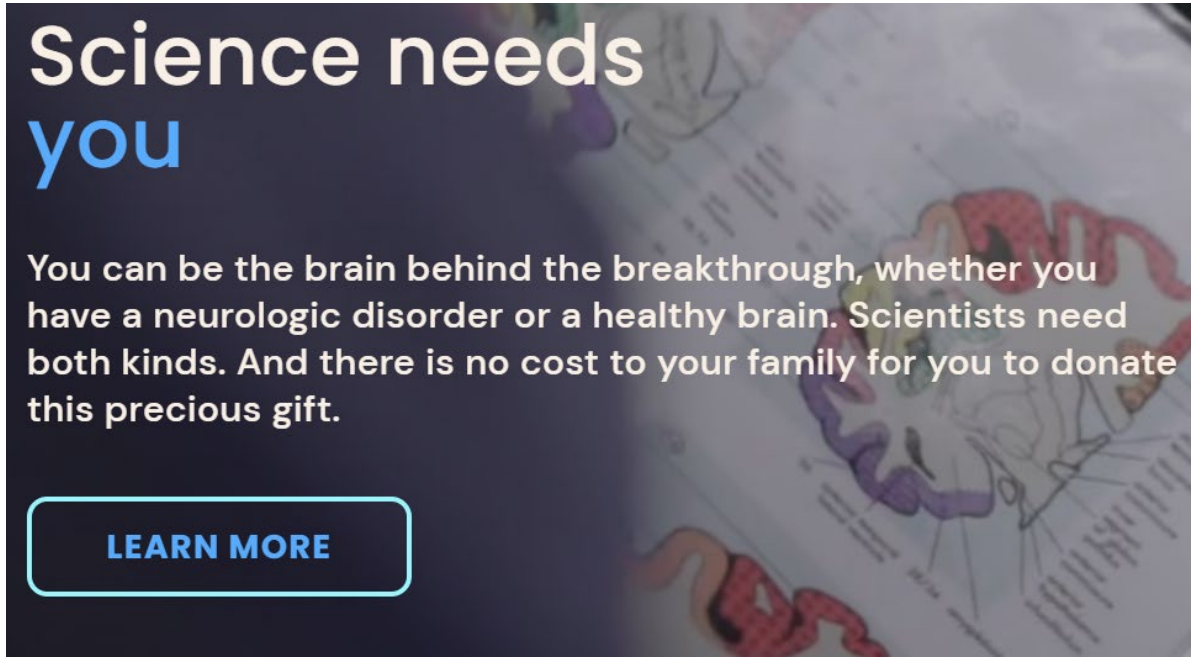
Working Group of ADRC NP Cores and NBB

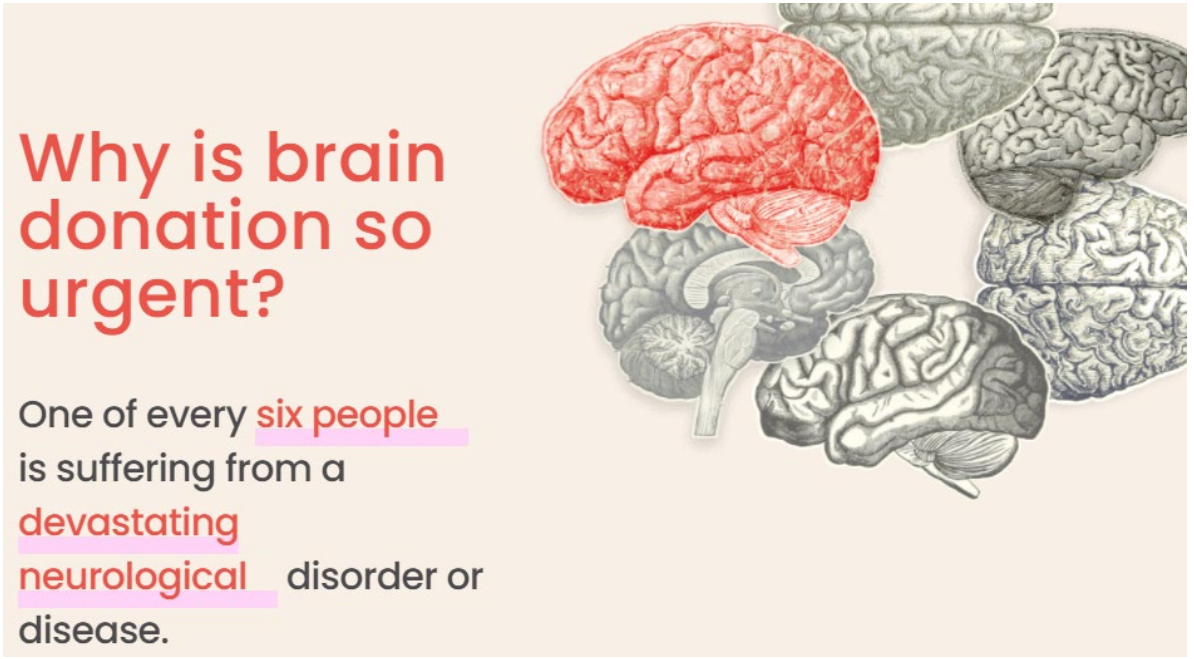
- Membership
  - **NIA:** Nina Silverberg, Erika Tarver, Grayson Donley
  - **NIMH:** Abigail Soyombo, Michelle Freund
  - **NINDS:** Daniel Miller, Anna Taylor
  - **BDP**: Tish Hevel
  - **NACC:** Walter Kukull, Maggie Dean, Merilee Teylan, Brian Stahly
  - **ADRC NP Cores:** Dirk Keene (UW), Anita Huttner (Yale), Julia Kofler (Pittsburgh)
  - **NBB:** Sabina Berretta (Harvard McLean), Harry Haroutunian (Mt. Sinai), and Bill Scott (Miami)
- Monthly meetings since July 2018

Pilot Project: Goals

- Demonstrate feasibility
  - Establish communication and coordination pipelines between donors, coordinators (TBDP, NBB, LBDA, etc.) and NP sites (NBB, NP Cores)
  - Build communication strategies for donors/families
    - To inform donors/families of benefits to science of donation (pretty much already done at TBDP)
    - To create harmonized strategies to relay neuropathologic findings to families of brain donors
  - Determine minimum and optimum clinical/other characterization criteria for brain donors (seen by a physician, psychometric data, imaging, genetics, etc.)
  - Develop program or site-specific inclusion/exclusion criteria
  - Develop central protocols to prioritize site selection for each donor
    - Geography
    - Prior participation in the Center
    - Site specific focus/emphasis (AD, TBI, etc.)
- Determine if donor coordination can improve frequency and utility of brain donation
- Identify areas of success and for improvement
- Extend to the broader research community

Brain Donor Project



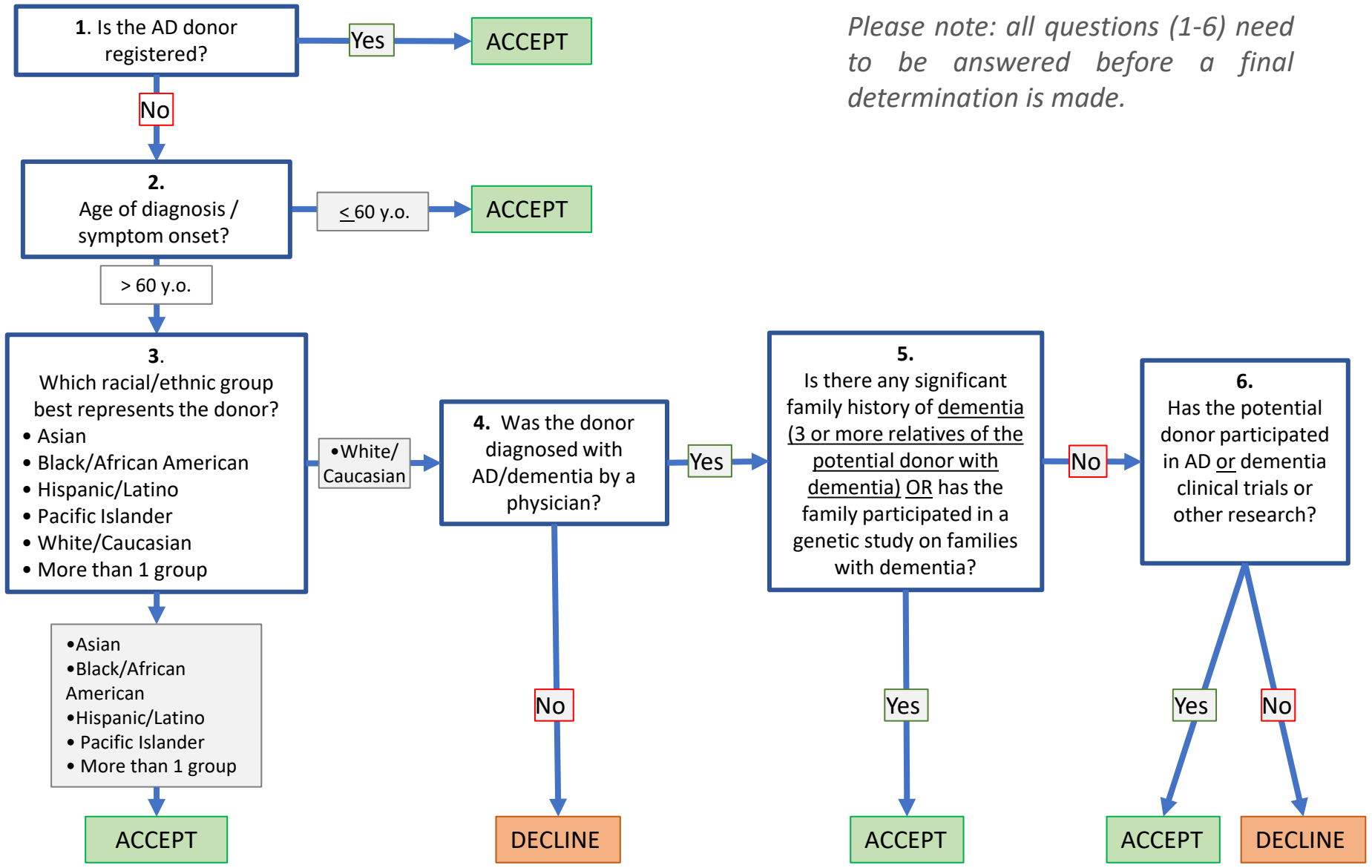


https://braindonorproject.org/

Slide courtesy of Dr. Nina Silverberg

NeuroBiobank: Alzheimer's Disease screening algorithm

Regardless of geographic location:



Please note: all questions (1-6) need to be answered before a final determination is made.

BDP Referral Algorithm for ADRC NP Cores

- Refer to NBB if:
  - Lewy body dementia
  - Frontotemporal dementia and related disorders
  - Parkinson's disease/PD w/dementia
  - Early onset of dementia symptoms
  - Past or current participation in clinical trial, research study or genetic testing
  - Significant family history (3 or more blood relatives with dementia)
  - Donor is part of an under-represented ethnic/racial group

- Refer to ADRC if:
  - Donor is within 100 mile radius of participating ADRC
  - Donor diagnosed with AD dementia by a clinician
  - Donor is a control
  - Also referred are donors with MCI, vascular dementia, or general dementia NOS

ADRC-NBB Pilot: Workflow

- With referral, pilot Center obtains consent for brain donation and makes arrangements as with other Center cohort subjects
- Upon death
  - Tissue/biofluid collection and banking
  - Follow up interview/questionnaire with family/LNOK
  - Neuropathology workup (Center protocol adhering to minimum standard)
  - Serology (blood)
  - Toxicology testing (blood or tissue)
  - Required data elements uploaded to NBB - IMS
  - Brief Data Set uploaded to NACC

ADRC-NBB Pilot: Workflow

- With referral, pilot Center obtains consent for brain donation and makes arrangements as with other Center cohort subjects
- Upon death
  - Tissue/biofluid collection and banking
  - Follow up interview/questionnaire with family/LNOK
  - Neuropathology workup (Center protocol adhering to minimum standard)
  - Serology (blood)
  - Toxicology testing (blood or tissue)
  - Required data elements uploaded to NBB
  - Brief Data Set uploaded to NACC

Progress to date (Pitt and UW)

				Clinical Diagnoses (if included)					
	Total	Male/Female	Demented	Controls	Age range	AD	LBD	PD	Vascular dementia
Consented	90	34/66	53	37	60-100	35	1	4	4
Donors	38	14/24	34*	1*	60-100	22	1	4	4
			*missing most recent cognitive information						

Progress to date (Pitt and UW)

Finalized Cases (n=28)				
		ADNC	n	Other Dx
Demented	27	High	25	FTLD, HS, LBD, uVBI, LATE, ARTAG
		Intermediate	2	HS, LBD, uVBI, LATE, ARTAG
		Low	0	
Non-demented	1	None	1	LBD

	LBD	n	
Demented	Neocortical	7	
	Limbic (transitional)	4	
	Brainstem	0	
	Amygdala	4	
	Not identified	11	
Non-demented	Neocortical	1	PD

	LATE stage	n
Demented	3	7
	2	7
	1	3
	0	10
Non-Demented	0	1

Pilot Project: Goals

- Demonstrate feasibility
  - Establish communication and coordination pipelines between donors, coordinators (TBDP, NBB, LBDA, etc.) and NP sites (NBB, NP Cores)
  - Build communication strategies for donors/families
    - To inform donors/families of benefits to science of donation (pretty much already done at TBDP)
    - To create harmonized strategies to relay neuropathologic findings to families of brain donors
  - Determine minimum and optimum clinical/other characterization criteria for brain donors (seen by a physician, psychometric data, imaging, genetics, etc.)
  - Develop program or site-specific inclusion/exclusion criteria
  - Develop central protocols to prioritize site selection for each donor
    - Geography
    - Prior participation in the Center
    - Site specific focus/emphasis (AD, TBI, etc.)
- Determine if donor coordination can improve frequency and utility of brain donation
- Identify areas of success and for improvement
- Extend to the broader research community

Tissue Sharing Proposal

- Tissues from NBB donors can be used for normal ADRC NP Core workflow - sharing
- Donor metadata listed with NBB; host ADRC considered as affiliate site
  - Investigators who land on ADRC-NBB pilot tissues through NBB are referred directly to the ADRC, which coordinates with the requestor
- Tissue sharing is through normal workflow for the local center
  - MTA development
  - Donor, region, tissue selection, etc.
- Sites update NBB periodically on tissue sharing/progress and if brain regions/samples become unavailable

Potential Benefits of Program

- **Promotes collaboration** across NBB, ADCs, BDN to set the foundation for enhanced national access for brain donation and brain research in AD, ADRD
- Allows both NBB and ADCs ability to accept **greater number and greater diversity of community-based AD** and control donations and make more biosamples and data available to the research community.
- Shared approaches/protocols can help **cross pollinate best practices** across programs
- **Improved and harmonized methods** to provide access to brain donors and scientists and for stakeholders to communicate with each other and donors/scientists.
- Increased ability for sites to retrieve registered cases outside of the pilot across programs (through NBB, NACC, local ADRC, etc.)
- Shared costs allow for greater collection of cases of interest to all parties
- Small catchment area and specific expertise of ADCs **allows for rapid autopsy and tissue processing for next generation research approaches**

Update: TBI-Related Neurodegeneration Neuropathology Common Data Elements (CDEs)

Neuropathology Working Group

- John Crary, MD, PhD, (co-chair), Icahn School of Medicine at Mt. Sinai
- Rebecca Folkerth, MD (co-chair), NYC Office of the Chief Medical Examiner
- C. Dirk Keene, MD, PhD (co-chair), University of Washington
- Russ Huber, MD, PhD, Boston University
- Julia Kofler, MD, University of Pittsburgh
- Gabor Kovacs, MD, PhD, University of Toronto
- Ann McKee, MD, Boston University
- Thor Stein, MD, PhD, Boston University
- William Stewart, PhD, Glasgow University
- Douglas Wiebe, PhD, U. Pennsylvania

Data Submission Testing Team

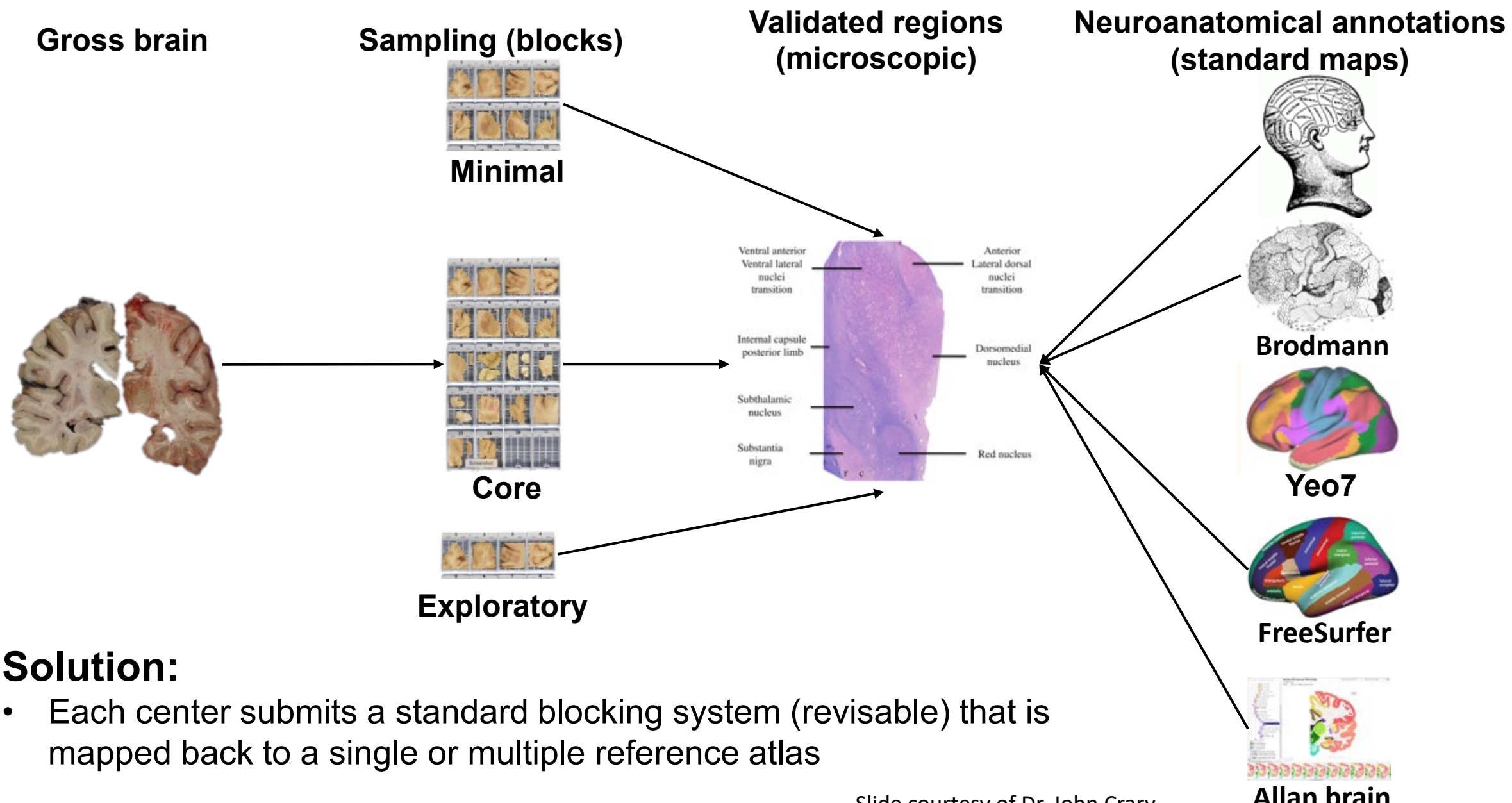
- Abigail Bretzin, PhD, University of Pennsylvania
- Kaitlyn Hartlage, MPH, Boston University
- Joseph Palmisano, MA, MPH, Boston University
- Douglas Wiebe, PhD, University of Pennsylvania

NIH/FITBIR

- Deborah Babcock, PhD, NINDS
- Patrick Bellgowan, PhD, NINDS
- Rebecca Berman, PhD, NINDS
- Rashida Kamara, BS, NINDS
- Kevin Armengol, MS, FITBIR data curator
- Olga Vovk, PhD, FITBIR data curator

https://fitbir.nih.gov/chronic-tbi-related-neurodegeneration-cdes

FITBIR
Federal Interagency Traumatic Brain Injury Research
INFORMATICS SYSTEM



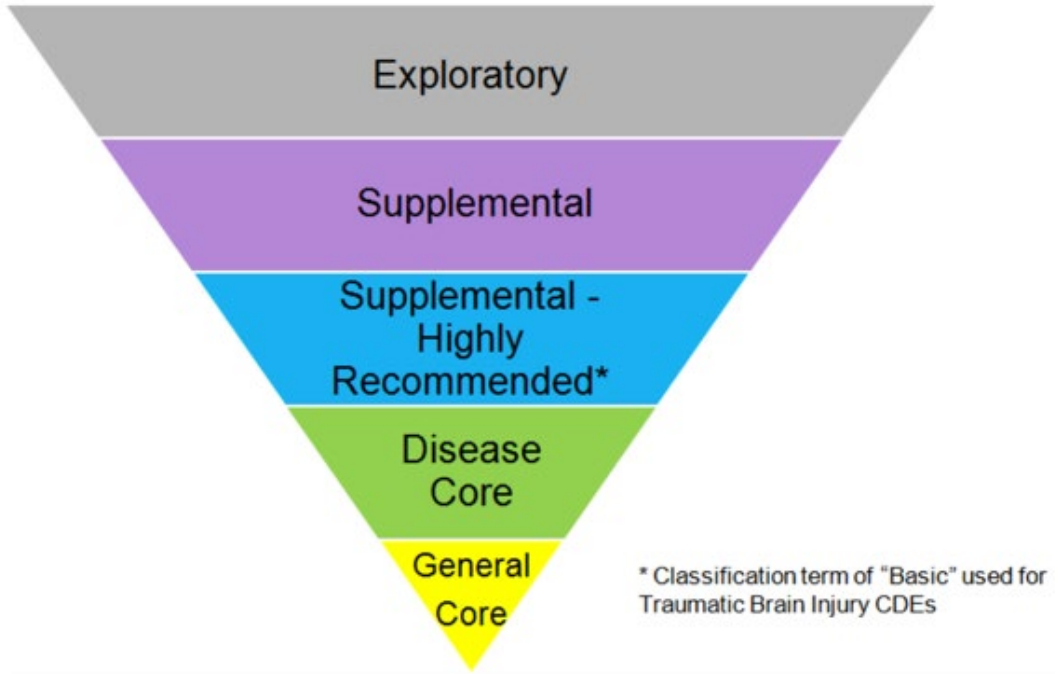
Solution:

- Each center submits a standard blocking system (revisable) that is mapped back to a single or multiple reference atlas

Slide courtesy of Dr. John Crary

Classification Scheme

- **Core**
  - Validated sampling for each category
  - NIA-AA recommended sampling and workup – NACC data structure
  - CTE consensus criteria (~14 blocks)
- **Supplemental highly recommended**
  - Sufficient material to render additional relevant NDD diagnoses
  - Ability to assess common co-morbid diagnoses
  - Validated sampling for each category
- **Supplemental**
  - Rare / less relevant neurodegenerative diseases
  - Inconvenient sampling (e.g., spinal cord, DRG, peripheral nerve)
- **Exploratory**
  - Research driven
  - Non-validated or unconventional brain regions



- **Summary:**
  - Top-Down Approach
  - Optional fields to permit recording novel sampling and neuropathological findings
  - Potential use as TBI supplement to NACC neuropathology CDE

Slide courtesy of Dr. John Crary

Comments/Questions