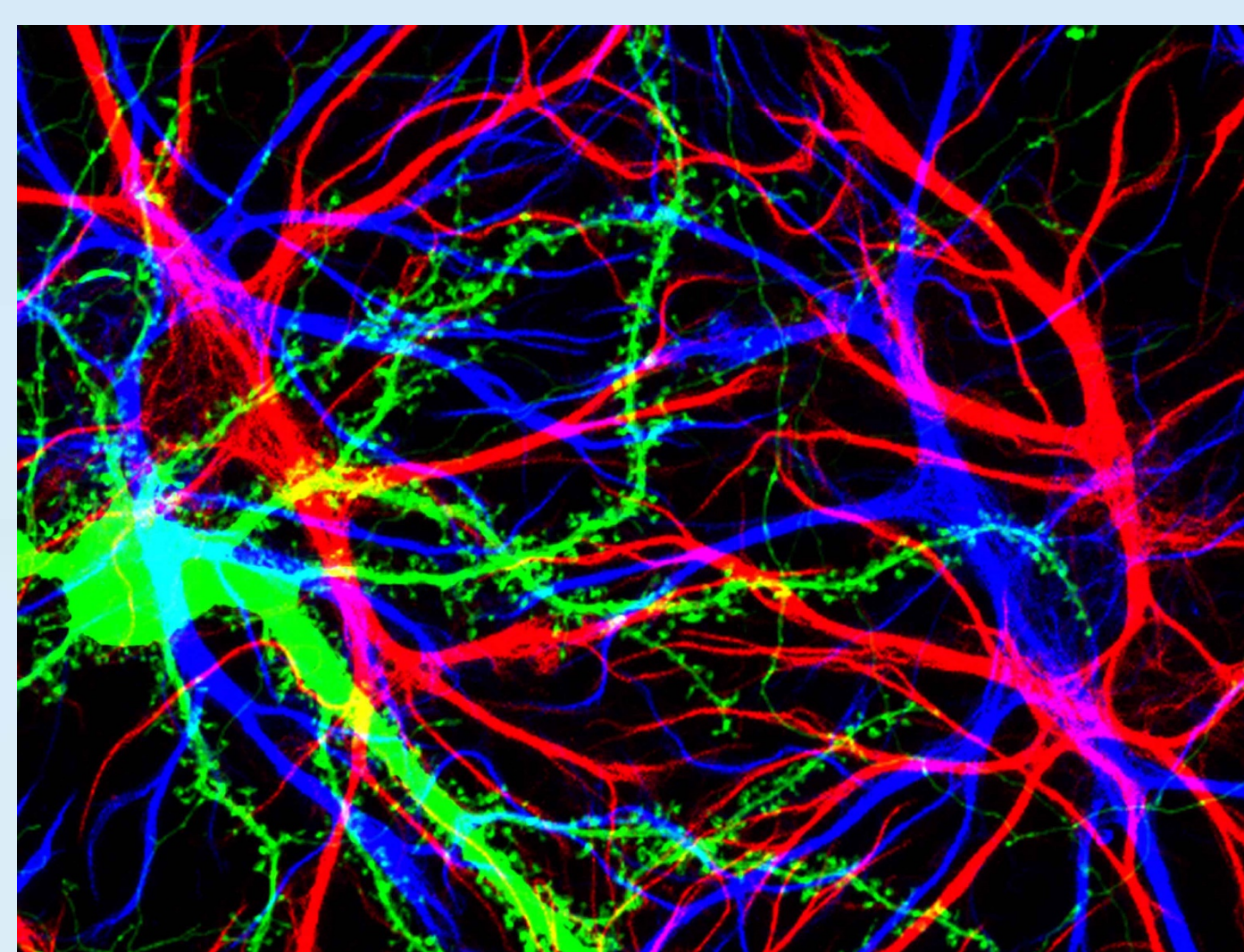


Background

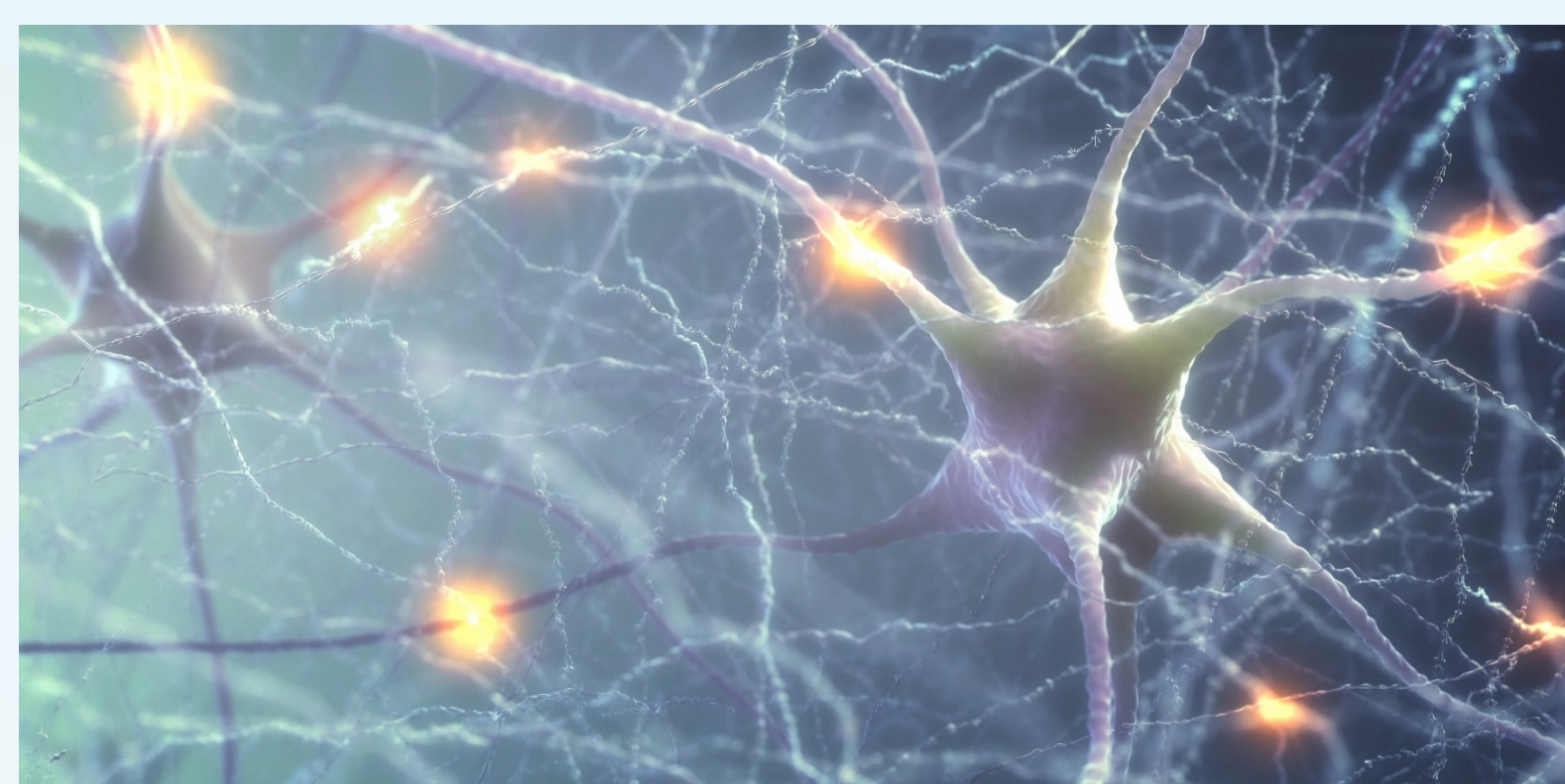
Advancing ASD Research: Studying human biospecimens is essential to advance our understanding of pathogenesis and treatment of neurological disease, including Autism Spectrum Disorders (ASD). The lack of suitable human biospecimens to conduct ASD research and develop new treatment options is a significant impediment for the field. More effective approaches and reliable sources of human biospecimens are needed to address this gap for the ASD research community. Here we report our efforts to address this gap and advance ASD research through supporting the development of a human tissue bank that provides high-quality human biospecimens to the ASD research community



Key Objectives:

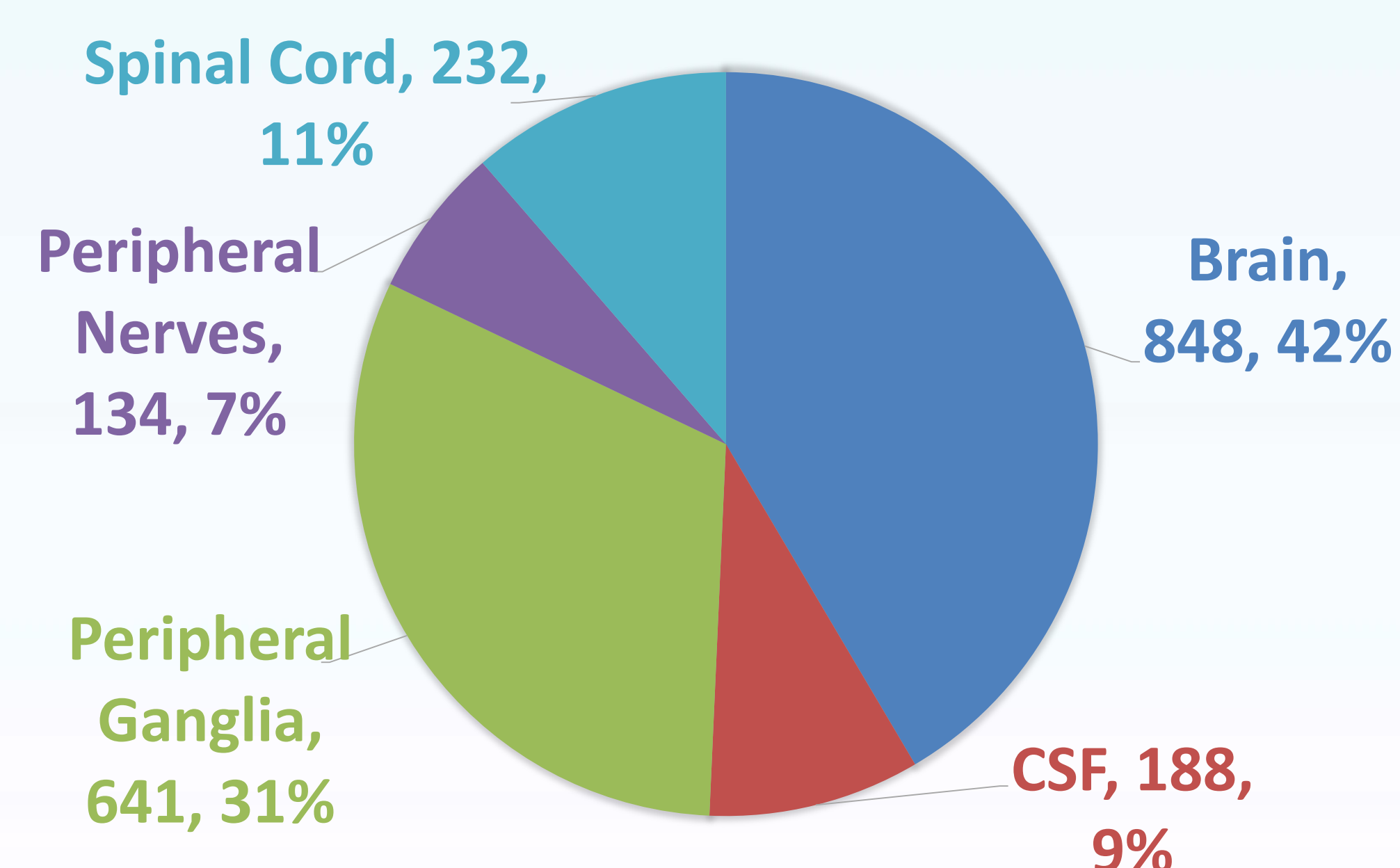
1. Discuss screening tools to identify, authorize, and recover biospecimens from ASD and normal control donors
2. Report on the need for greater access to human neurological biospecimens

NDRI Contributes to Neurological Disease Research Through Human Tissue and Organ for Research Resource (HTORR)



- NDRI's HTORR program has been funded by the NIH for > 30 years
- Through HTORR, NDRI supports a range of neurological research

Brain Is Our Leading Neurological Biospecimen Placement



NDRI provides a range of neurological tissues to investigators worldwide: The pie chart indicates the types of neurological tissue placed by NDRI in the last 5 years from TSS partners. Brain continues to be the most requested tissue type. Tissues placed include those from normal as well as diseased donors (including Alzheimer's disease, ALS, depression, PTSD, and spinal cord injury).

Autism Spectrum Disorder (ASD) Research Requires Human Tissue Donation

Project Performance

ASD Donors	Normal Control Donors
30	5

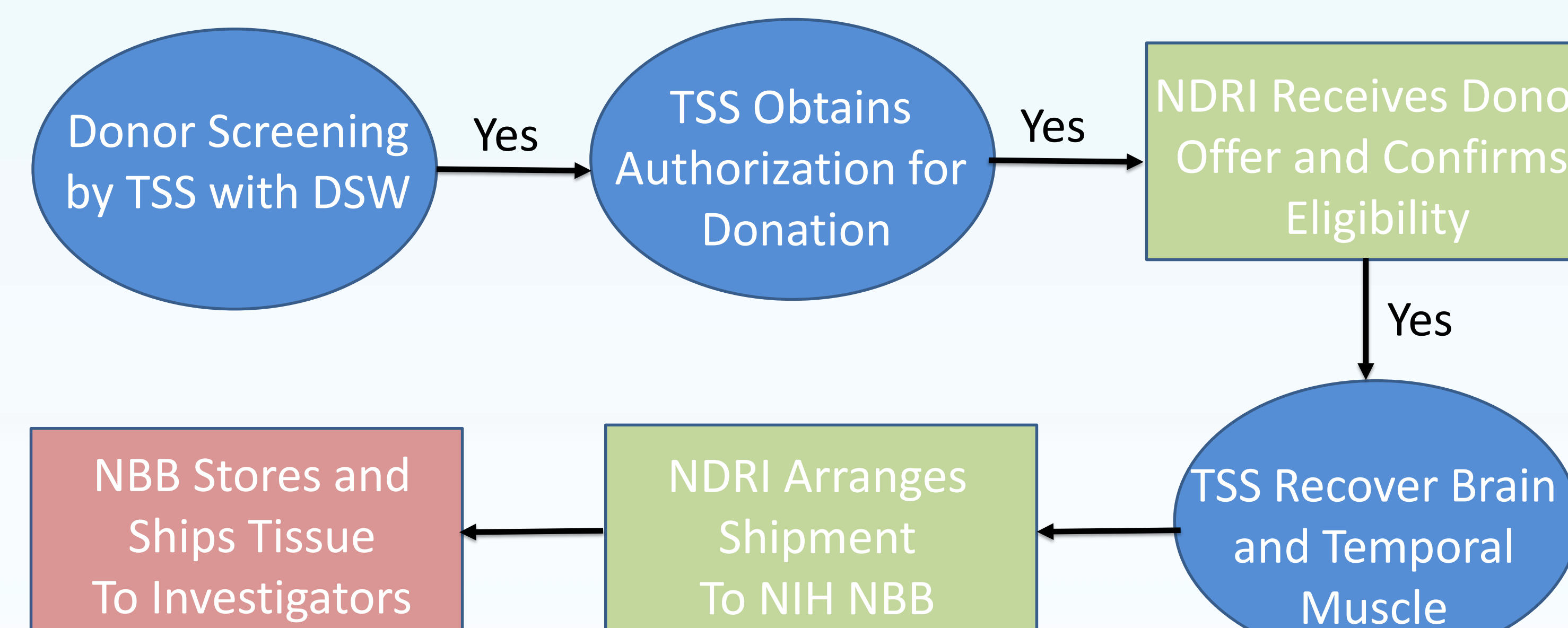
- Funded by the National Institute of Mental Health (NIMH) through a supplement to HTORR
- Currently in Program Year 4
- Brain and temporal muscle recovered from ASD and normal pediatric control donors at 14 TSS

Identifying ASD and Normal Pediatric Control Donors Requires Enhanced Donor Screening

ASD Donors	Normal Controls
Age > 2	Age 2-18
ASD diagnosis (Autism, Asperger's, or Pervasive Dvpt Disorder)	No neurological disorders
No chemo/radiation in past 24 months	No chemo/radiation in past 24 months
No sepsis at time of death	No sepsis at time of death
Ventilator < 24 hours	Ventilator < 24 hours
Collection must occur within 24 hours of cardiac cessation	Collection must occur within 24 hours of cardiac cessation

NDRI's Brain Donor Screening Worksheet (DSW) Enables Identification of Critical Donation Opportunities: NDRI developed a donor screening worksheet (DSW) utilized by all partnering OPOs to clearly rule potential brain donors in or out for the ASD project. OPO staff use the DSW for each potential brain donor. If a donor is eligible, OPOs approach NOK for authorization. Eligibility criteria are shown in the table above.

NDRI and TSS Partners Are Essential For the Success of the ASD Program



NDRI's Partnering TSS Serve as the Link Between Donors and the Advancement of ASD Research: NDRI partners with 14 tissue source sites (TSS) that screen all brain donation opportunities using the ASD Project DSW, work with next-of-kin to obtain authorization for donation specifically for the ASD Project, and recover tissues from eligible donors. NDRI coordinates shipment to the NIH NeuroBioBank (NBB) where tissue is stored and distributed to approved investigators studying the pathophysiology of ASD.

The NIH NeuroBioBank Facilitates Cutting-edge ASD Research by Providing Access To Valuable Donated Specimens



The impact of the resource is evident by high-impact investigator publications, including:

- Velmeshev D, et al. Single-cell genomics identifies cell type-specific molecular changes in autism. *Science*. 2019 May 17;364(6441):685-689.
- Avino TA, et al. Neuron numbers increase in the human amygdala from birth to adulthood, but not in autism. *PNAS* 2018 Apr 3: 115 (14): 3710-3715.
- Wang Z, et al. Amelioration of autism-like social deficits by targeting histone methyltransferases EHMT1/2 in Shank3-deficient mice. *Molecular Psychiatry* 2019

Meeting Unmet Needs of the AD/ADRD Research Community

Alzheimer's Disease Biospecimen Resource (ADBR)

- Identify the donor criteria and biospecimens of greatest need with an ADBR Advisory Council
- Collaborate with TSS to develop methods for screening, authorizing, and recovering biospecimens from eligible AD/ADRD donors



Supplemental HTORR Funding Will Support a Resource for Alzheimer's Disease and Related Dementias (AD/ADRD) Research: The National Institute of Aging (NIA) at NIH awarded NDRI a supplement to its HTORR program to create a new human biospecimen resource, the ADBR, to support AD/ADRD research. NDRI leads an advisory council made up of NIH, academic, and industry leaders in the field whose goal is to identify the areas of greatest need within AD/ADRD research.

Summary:

1. ASD investigators require greater access to human brains to expand our understanding of pathophysiology of ASD and develop new treatments
2. The NIH's NeuroBioBank partnership with NDRI expands their reach to screen and recover ASD donation opportunities to support a diverse range of studies
3. NDRI is building upon their established ASD donation model to support other neurological biospecimen needs for the research community

Acknowledgements

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- Partnering TSS (Center for Organ Recovery and Education, Dakota Lions Sight and Health, Donor Network West, Gift of Life Donor Program, LifeGift, LifeLink Foundation, LifeNet Health, Mid-America Transplant, Unyts, Washington Regional Transplant Center)
- NDRI would also like to thank the donors and their families for providing valuable donations to advance ASD research.