

NeuroBooster Array: Update



NeuroBooster Array: Overview

- **NeuroBooster = GDA (1.9M variants) + NDD related content (95K variants)**
 - NDD related content can be also combined with MEG or GSA.
- **GDA includes genetic markers gathered from individuals of diverse ethnic groups**
 - African Americans, Hispanics, Pacific Islanders, East Asians, admixed ancestry

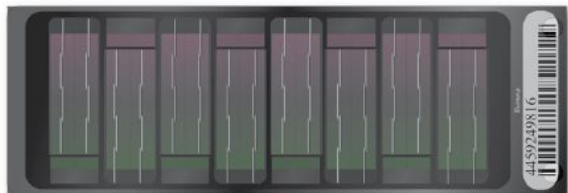


Figure 1: Infinium Global Diversity Array-8 v1.0 BeadChip—Built on the trusted 8-sample Infinium platform.

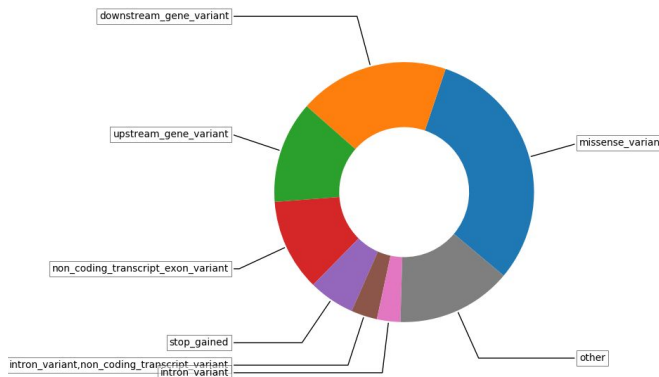
NeuroBooster Array: Aims



- Generally improve imputation quality across populations of diverse continental ancestries to facilitate risk loci discovery.
- Improve imputation of known GWAS loci for NDDs across populations of diverse ethnicity to facilitate trans-ethnic studies.
- Identify coding and low frequency variants of interest to researchers on the NDD field.

NeuroBooster Array: Design

- **STEP 1: Selection of tagging NDD related coding & low frequency variants**
 - Systematic review on the **Human Genome Mutation Database**
 - **Genomics England disease-specific expert panels** in concert with Gnomad
 - **IPDGC and CARD collaborators**



NeuroBooster Array: Design



- **STEP 2: Identification of the best multi-population tag SNPs**
 - **AMR** <-- MXL, CLM, PEL, PUR (**Latino ancestry populations**)
 - **EAS** <-- JPT, CDX, CHB, CHS, KHV, CHD (**East Asian populations**)
 - **EUR** <-- TSI, IBS, GBR, CEU (**European populations, note the FIN are excluded as outliers in PCA**)
 - **SAS** <-- PJI, ITU, STU, GIH, BEB (**South Asian populations**)
 - **AFR** <-- GWD, MSL, ESN, GWJ, YRI, LWK, GWF, GWW (**African populations**)
 - **AAC** <-- ASW, ACB (**African American and Caribbean populations**)
- ** LD comparisons and allele frequency calculation**

NeuroBooster Array: Design



- **STEP 3: Dense selection of tag SNPs within NDD GWAS regions.**

199 NDD related loci

- **AD:** Jansen et al, 2019, Kunkle et al, 2019
- **PD:** Nalls et al, 2019 and **PD progression** Iwaki et al, 2019
- **ALS:** Nicolas et al, 2019
- **DLB:** Guerreiro et al, 2018, **PSP:** Hoglinger et al, 2011, **FTD:** Ferrari et al, 2014

** 1809 PRS SNPs nominated by PRSice

- **STEP 4: Imputation boosters for diverse populations.**

NeuroBooster Array: Imputation

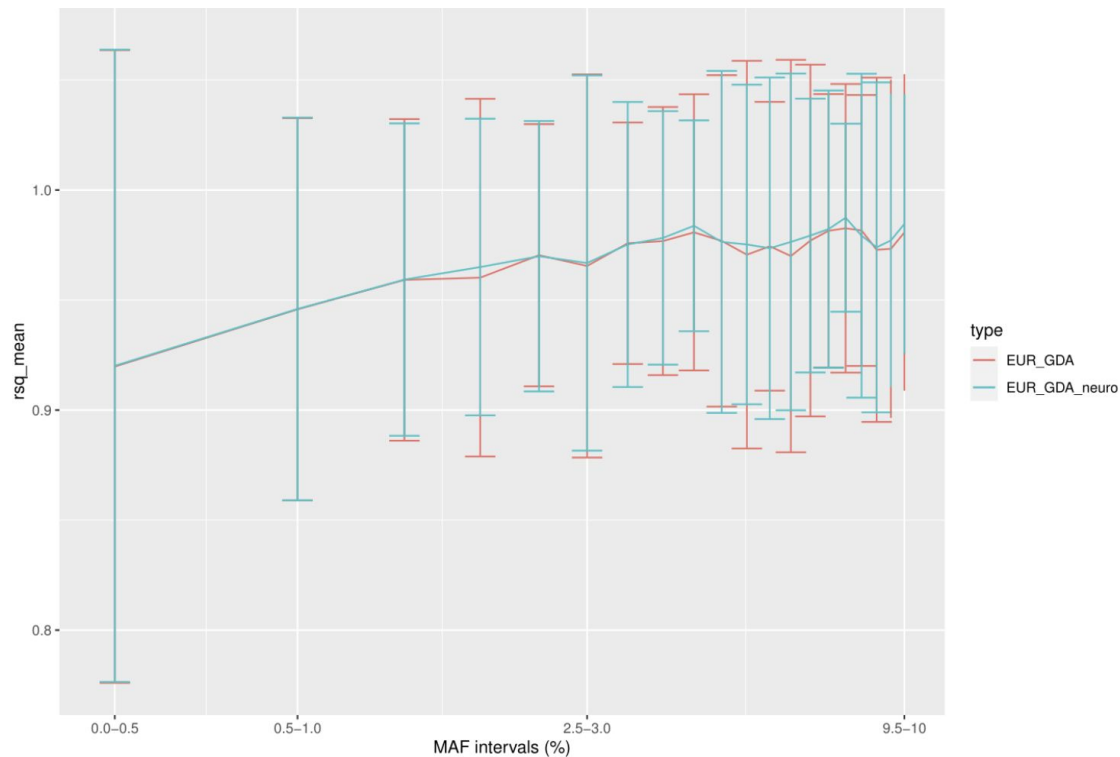


- **WGS data from six 1000 Genomes populations**
 - AAC (157), AFR (504), AMR (347), EAS (504), EUR (404), SAS (489)
- **Extract only GDA content -> Imputation**
- **Extract GDA + Neuro content -> Imputation**
- **Imputation versus various panels**
 - HRC, CAAPA, GAsP, TopMed
- **Imputation performance for the 199 NDD related loci**
 - GDA content *versus* GDA + Neuro content

NeuroBooster Array: Imputation

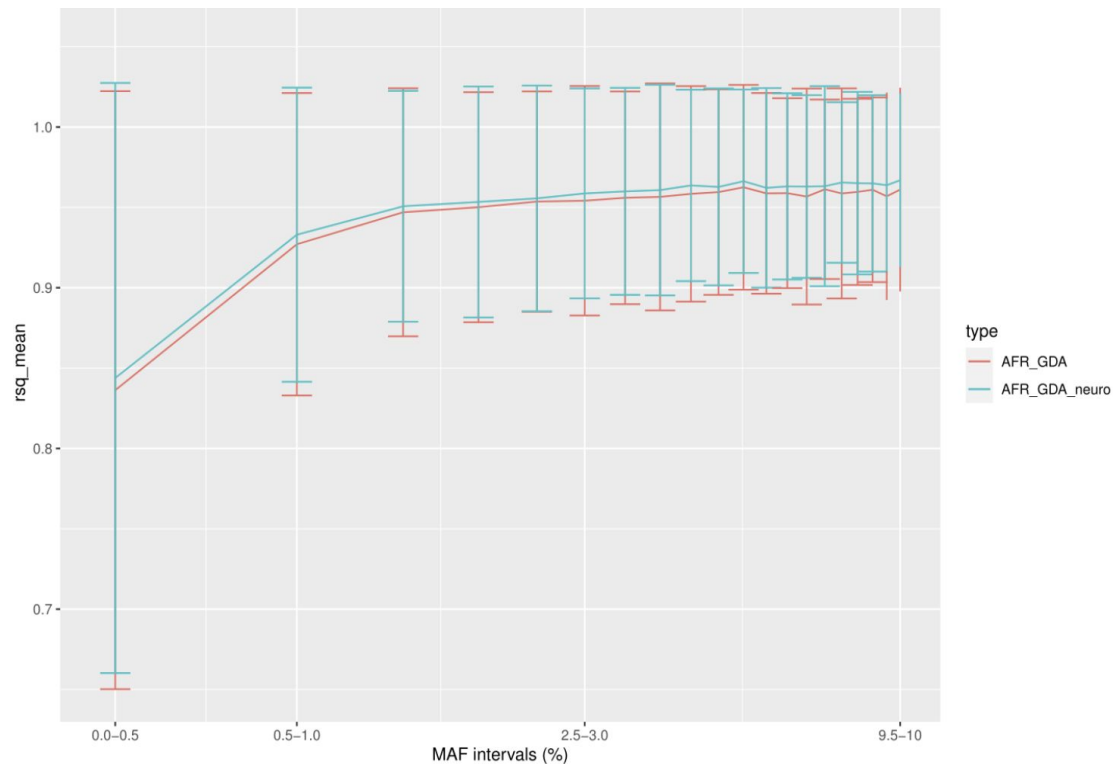


EUR population
(HRC panel)



NeuroBooster Array: Imputation

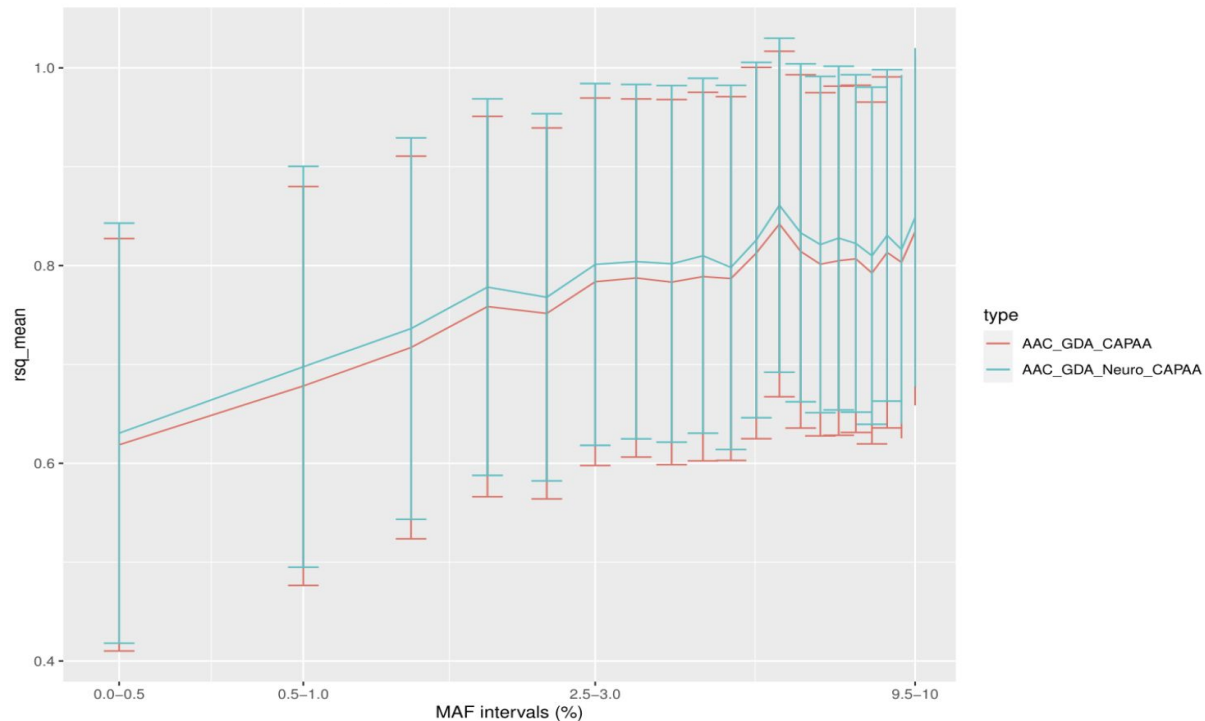
AFR population
(CAAPA panel)



NeuroBooster Array: Imputation

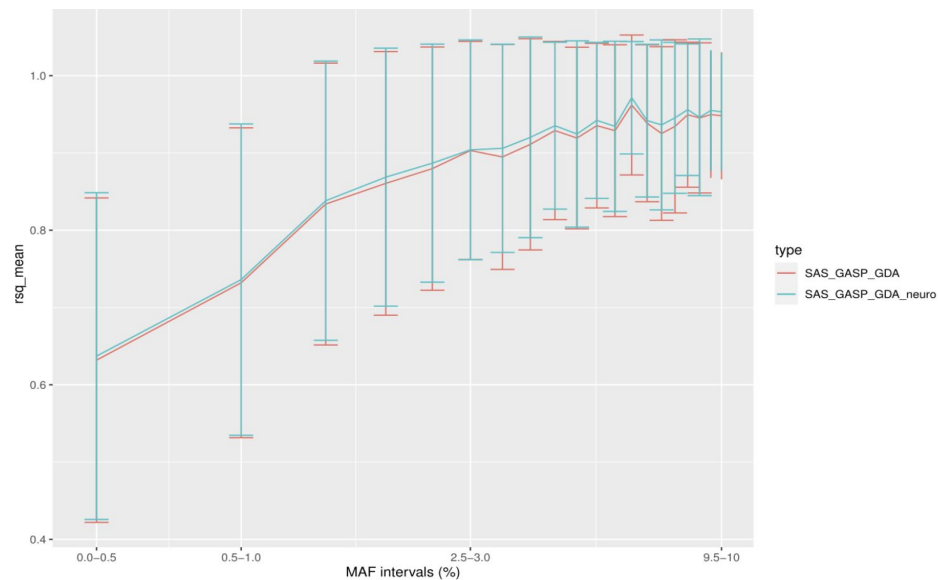
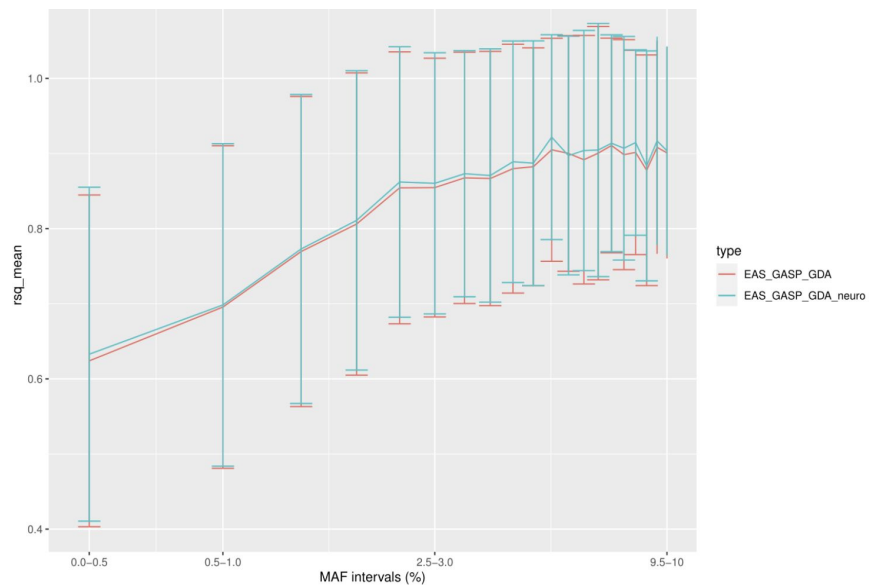


AAC population
(CAAPA panel)



NeuroBooster Array: Imputation

SAS & EAS populations (GAsP panel)



NeuroBooster Array: Imputation



AMR populations (HRC panel *versus* GAsP panel *versus* CAAPA panel)

