The American Journal of Human Genetics, Volume *109*

Supplemental information

Rare genetic variants in genes and loci linked to dominant monogenic developmental disorders cause milder related phenotypes in the general population

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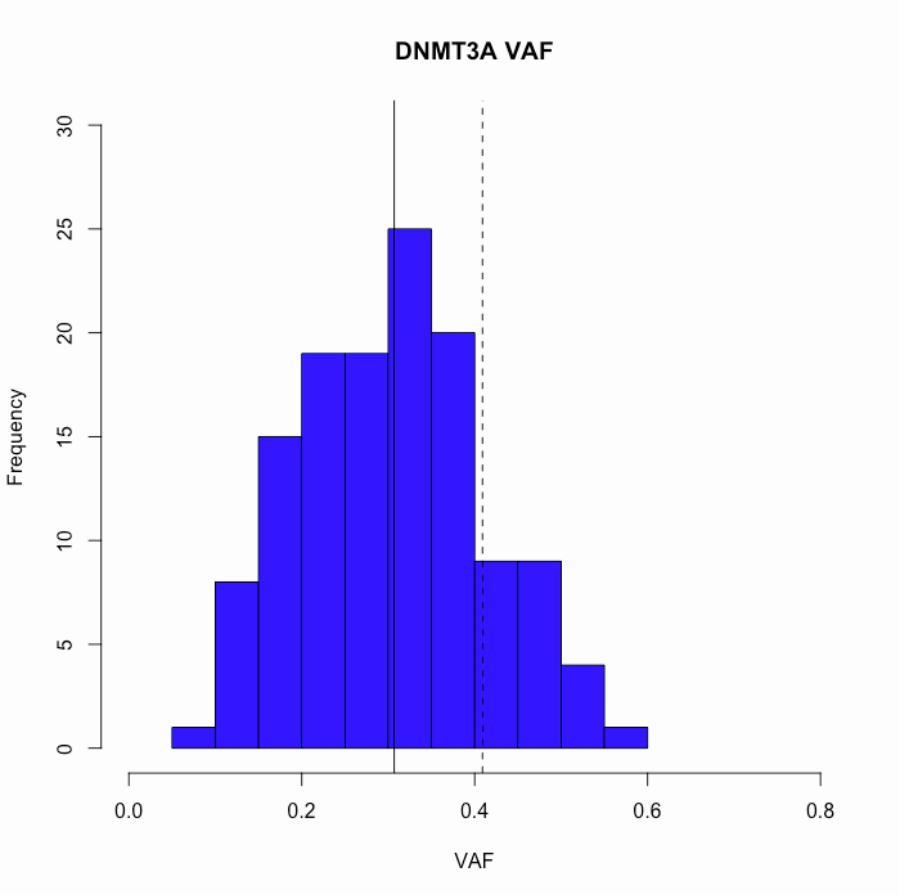
Supplementary Information

Supplementary Figures

Supplementary Figure 1: Histogram showing the Variant Allele Fraction (VAF) of variants located in *DNMT3A*, dashed line indicating the average VAF of variants in other genes, with filled line showing the average VAF of variants in *DNMT3A*.



Supplementary Tables

Included in an Excel file.

Worksheet 1: Known monoallelic DDG2P genes

Worksheet 2: Copy number variants in UKB overlapping 69 known DD loci

Worksheet 3: Gene panel association tests for LoF variants across different gene subsets

Worksheet 4: Gene panel association tests for deleterious missense variants across different CADD bins

Worksheet 5: Gene panel association tests excluding individuals diagnosed with a childhood developmental disorder

Supplementary Methods

STATA code: Logistic regression

```
<import UKB BOLT phenotype file>
<import UKB exome file>
<import pcs file>
<import list of traits to test - varlist>

#varlist includes following traits: employed degree infertile epilepsy_ukbdef ChildDD_any
AdultDD_any unable_to_work

#for LoF variants:
generate variant = 1 if v2 == “lof_variant”
generate dont_use = 1 if v2 == “missense_variant”
replace variant = 0 if variant != 1
replace dont_use = 0 if dont_use != 1

file open myfile using <file_to_save_to>,
write append
set more off

foreach var of varlist {
        logistic `var' variant centre sex age_base pcs* if valid_exome =1 & dont_use != 1

file write myfile "`var'" _tab (r(table)[1,1]) _tab (r(table)[2,1]) _tab (r(table)[4,1]) _tab
(r(table)[5,1]) _tab (r(table)[6,1]) _n
}

file close myfile
```

STATA code: Linear regression

```
<import UKB BOLT phenotype file>
<import UKB exome file>
<import pcs file>
<import list of traits to test - varlist>

#varlist includes following traits: fluid_intelligence edu_yrs income reaction_time_raw_sin
pairs_test tdi age_education height mental_health numeric_memory_raw_sin
bmi_2016_raw_sin kids_fathered all_preg n_stillbirth

#for LoF variants:
generate variant = 1 if v2 == “lof_variant”
generate dont_use = 1 if v2 == “missense_variant”
replace variant = 0 if variant != 1
replace dont_use = 0 if dont_use != 1
```

```
file open myfile using <file_to_save_to>,
write append
set more off

foreach var of varlist {
        regress `var' variant centre age_base sex pcs* if valid_exome = 1 & dont_use != 1

file write myfile "`var'" _tab (r(table)[1,1]) _tab (r(table)[2,1]) _tab (r(table)[4,1]) _tab
(r(table)[5,1]) _tab (r(table)[6,1]) _n
}

file close myfile
```