

EDA: MS ComBat-GAM

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Objective

To visualize effects of ComBat-GAM applied on the MS data relative to the raw MS data.

IMPORTANT

MS patients from the *HSC* site that were scanned in a *SIEMENSTIMTRIO* scanner were excluded from the current harmonization.

[1] "In MS:"

	CHP	HSC
SIEMENSPRISMAFIT	0	28
SIEMENSTIMTRIO	0	18
SIEMENSVERIO	21	0

IMPORTANT (cont.)

The corresponding group in the Healthy Control data was similarly excluded when modeling site effects with ComBat-GAM.

[1] "In HC:"

	CHP	HSC	PNC
SIEMENSPRISMAFIT	0	58	0
SIEMENSTIMTRIO	0	7	1185
SIEMENSVERIO	36	0	0

1

Datasets: MS

MS (dimensions):

[1] 49 160

MS (count by site)

site	n
CHP	21
HSC	28

MS (count by sex)

sex	site	n
FEMALE	CHP	18
FEMALE	HSC	17
MALE	CHP	3
MALE	HSC	11

Datasets: HC

Dimensions HC (no PNC):

```
## [1] 94 160
```

Count per site:

site	n
CHP	36
HSC	58

Count by sex and site:

site	sex	n
CHP	FEMALE	24
CHP	MALE	12
HSC	FEMALE	37
HSC	MALE	21

Totals: Females 61; Males 33

Datasets: HC + MS

Dimensions (no PNC):

[1] 143 160

Count per site:

site	n
CHP	57
HSC	86

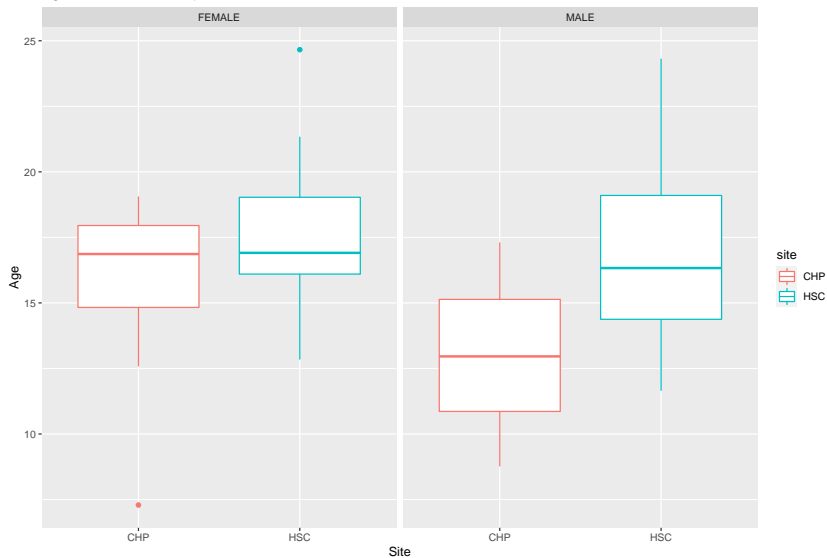
Count by sex and site:

site	sex	n
CHP	FEMALE	42
CHP	MALE	15
HSC	FEMALE	54
HSC	MALE	32

Totals: Females 61; Males 33

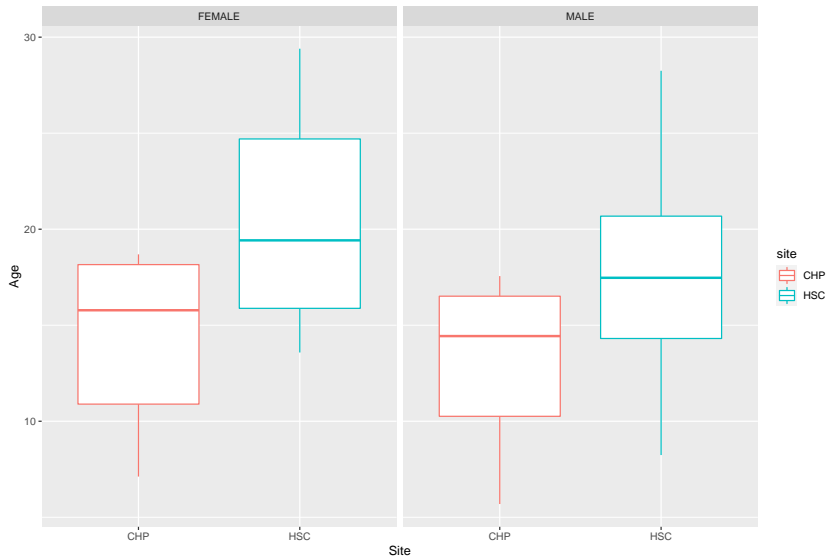
Age across sites [MS]

Age distribution of MS patients across sites



Age across sites [HC]

Age distribution of Healthy Controls across sites



Harmonization Approach

Adjusted data are shown for the following approach:

- * Split the HC data into males and females
- * Run ComBat-GAM on both datasets.
- * Apply resulting models to MS data in males and females respectively.

Checking site effects

Site effects were tested with different models and data splits.

For full datasets, either sex and interactions terms ($x \sim \text{sex} + \text{age} + \text{age}^2 + \text{age} \times \text{sex} + \text{age}^2 \times \text{sex}$) were included or only age terms ($x \sim \text{age} + \text{age}^2$).

For datasets split by sex, only age terms were included.

Site effects: MS [split M/F]

Number of ROIs showing site effects:

Full covariate model:

FDR	Bonferroni	Uncorrected
		P
6	1	37

Sex not considered:

FDR	Bonferroni	Uncorrected
		P
0	0	4

Site effects: MS [no split]

Full covariate model:

FDR	Bonferroni	Uncorrected
		P
19	2	43

Sex not considered:

FDR	Bonferroni	Uncorrected
		P
0	0	8

Site effects by sex: MS [M/F split]

Females:

FDR	Bonferroni	Uncorrected
		P
0	0	20

Males:

FDR	Bonferroni	Uncorrected
		P
29	2	49

Site effects by sex: MS [no split]

Females:

FDR	Bonferroni	Uncorrected
		P
0	0	20

Males:

FDR	Bonferroni	Uncorrected
		P
29	2	49

Site effects: HC [split M/F]

Full model:

		Uncorrected
FDR	Bonferroni	P
0	0	0

Sex not considered:

		Uncorrected
FDR	Bonferroni	P
0	0	0

Site effects: HC [no split]

Number of ROIs showing site effects:

Full model:

FDR	Bonferroni	Uncorrected
		P
0	0	0

Sex not considered:

FDR	Bonferroni	Uncorrected
		P
0	0	0

Site effects by sex: HC [split M/F]

Females:

FDR	Bonferroni	Uncorrected
		P
0	0	9

Males:

FDR	Bonferroni	Uncorrected
		P
0	0	10

Site effects by sex: HC [no split]

Females:

FDR	Bonferroni	Uncorrected
		P
0	0	9

Males:

FDR	Bonferroni	Uncorrected
		P
0	0	10

Conclusions

Harmonization seems to be effective for Females in HC and MS.

With the current approach, MS Males are not harmonized correctly.