Phase 3: Subject-to-Template Evaluation

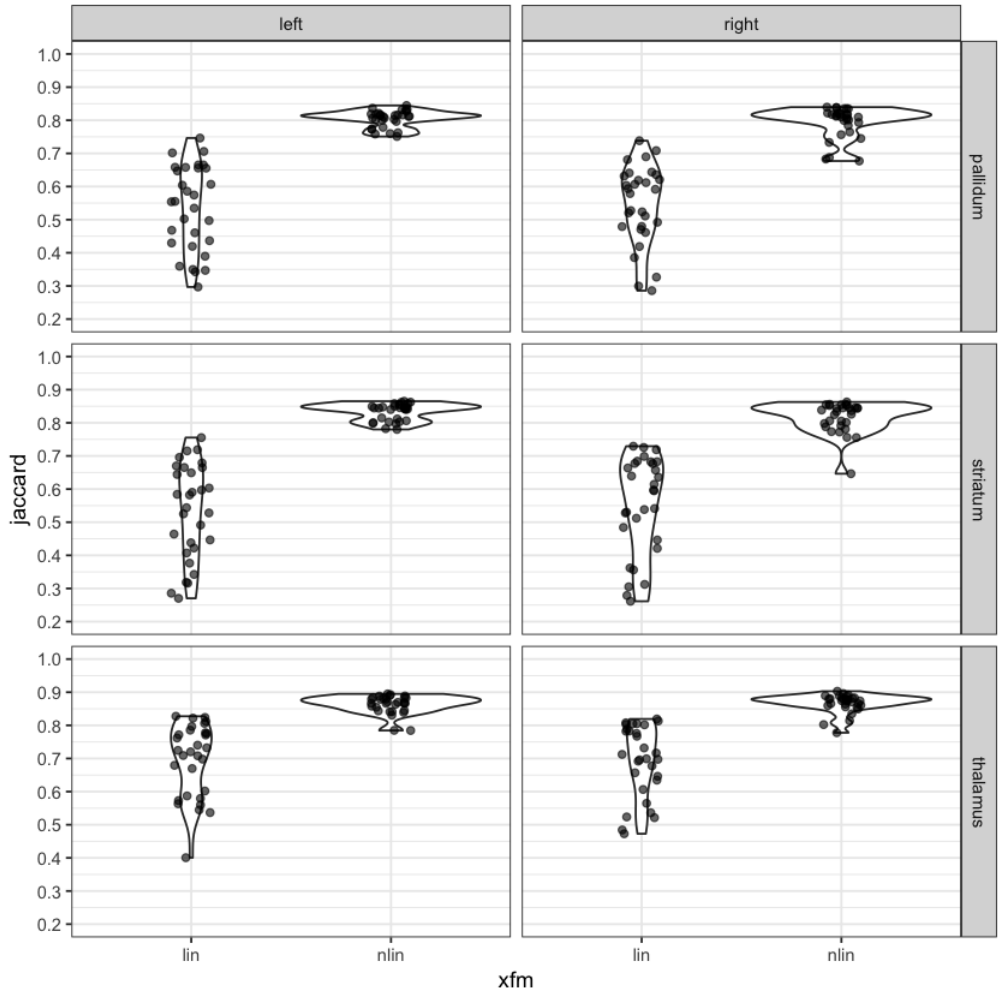
This notebook compares voxel overlap measures against AFID-based metrics for evaluating spatial correspondence. The OASIS-1 dataset from from PHASE2 was processed using the Ants-based T1-to-MNI (`MNI152NLin2009bAsym`) registration workflow built-in to fMRIPrep.

```
Attaching package: 'dplyr'

The following objects are masked from 'package:plyr':

    arrange, count, desc, failwith, id, mutate, rename, summarise,
    summarize

The following objects are masked from 'package:stats':

    filter, lag

The following objects are masked from 'package:base':

    intersect, setdiff, setequal, union

Loading required package: magrittr

Attaching package: 'ggpubr'

The following object is masked from 'package:plyr':

    mutate
```

ROI Overlap

Values for pallidum, striatum, and thalamus.

roi	side	jaccard_lin	jaccard_nlin	jaccard_lin_vs_nlin	kappa_lin	kappa_nlin	kappa_lin_vs_nlin
pallidum	left	0.54±0.13	0.80±0.03	*	0.69±0.11	0.89±0.02	*
pallidum	right	0.55±0.12	0.79±0.05	*	0.70±0.11	0.88±0.03	*
striatum	left	0.53±0.14	0.83±0.03	*	0.68±0.13	0.91±0.02	*
striatum	right	0.55±0.15	0.82±0.05	*	0.70±0.13	0.90±0.03	*
thalamus	left	0.70±0.11	0.86±0.03	*	0.82±0.08	0.93±0.02	*
thalamus	right	0.69±0.11	0.87±0.03	*	0.81±0.08	0.93±0.02	*


left
right
pallidum
striatum
thalamus
jaccard
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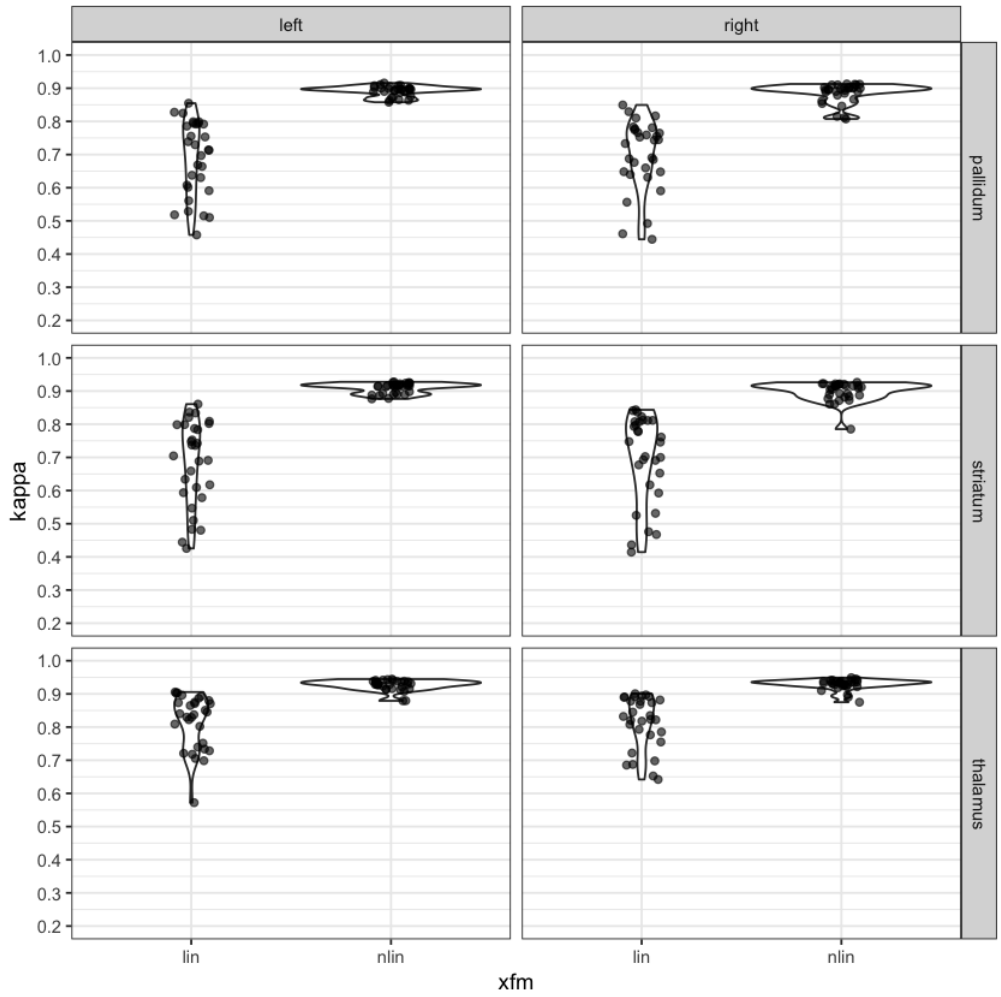
0.2
lin
nlin
xfm



AFRE

Anatomical FRE is evaluated here as a metric for looking at the spatial correspondence between images. Here they are summarized globally, for each AFID, and for each subject. Qualitatively, the ventricles are misaligned for OAS1_0109 which accounts for the maximally error observed in this analysis of > 30 mm AFRE.

Nonlinear Transform Results

'Total: 1.80 +/- 2.09 mm; Range: 0.07-32.78'

'Mean Max: 7.55 mm'

Linear Transform Results

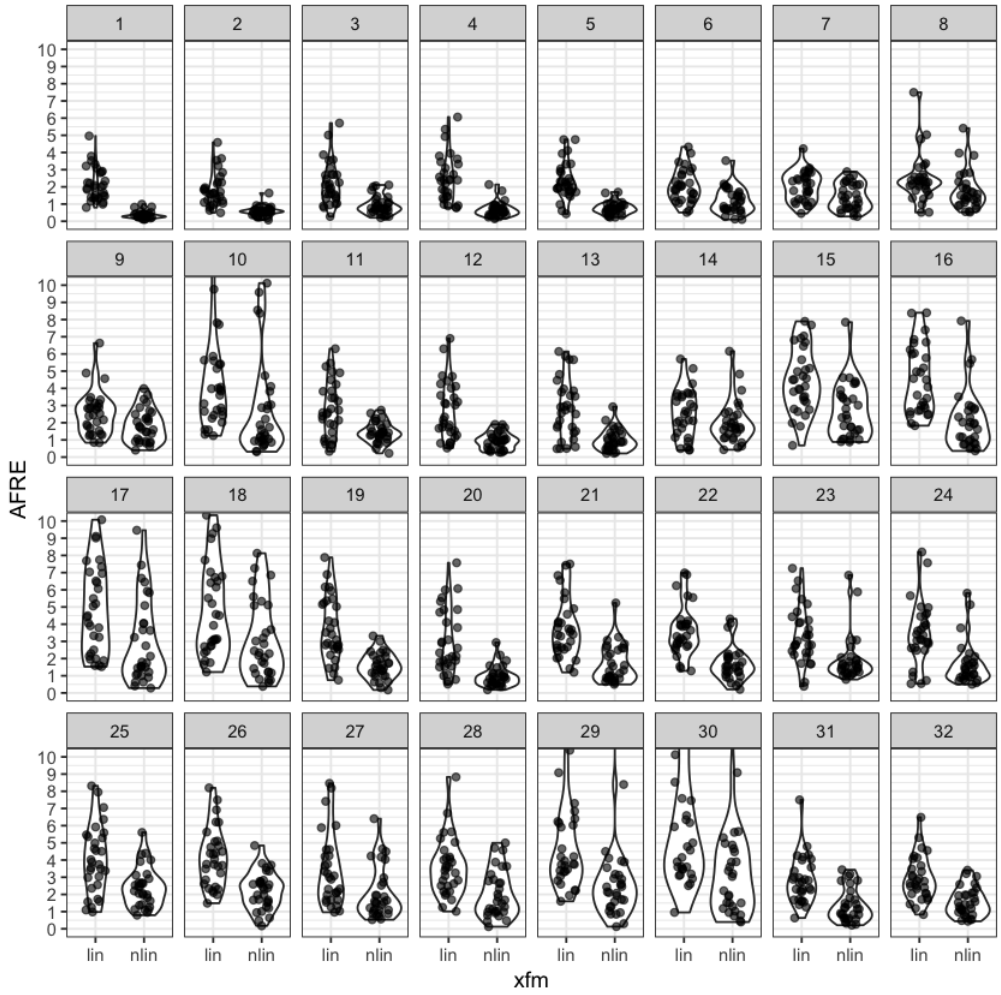
'Total: 3.40 +/- 2.55 mm; Range: 0.28-36.26; Mean Max: '

'Mean Max: 10.25 mm'

```
        Wilcoxon rank sum test with continuity correction

data:  df_subjects_lin$AFRE and df_subjects_nlin$AFRE
W = 716930, p-value < 2.2e-16
alternative hypothesis: true location shift is not equal to 0
```

AFID	Description	Mean AFRE lin	Mean AFRE nlin	lin vs nlin
01	AC	2.15±0.97 (4.96)	0.36±0.21 (0.99)	*
02	PC	1.83±0.96 (4.58)	0.57±0.29 (1.64)	*
03	infracollicular sulcus	2.20±1.23 (5.71)	0.93±0.53 (2.11)	*
04	PMJ	2.50±1.36 (6.06)	0.68±0.43 (2.13)	*
05	superior interpeduncular fossa	2.35±1.06 (4.75)	0.76±0.37 (1.69)	*
06	R superior LMS	2.07±0.95 (4.32)	1.17±0.74 (3.52)	*
07	L superior LMS	2.03±0.85 (4.22)	1.43±0.77 (2.88)	*
08	R inferior LMS	2.45±1.37 (7.50)	1.78±1.11 (5.41)	*
09	L inferior LMS	2.54±1.26 (6.63)	1.83±0.96 (3.99)	*
10	culmen	4.50±2.93 (12.72)	2.73±2.81 (10.12)	*
11	intermammillary sulcus	2.81±1.62 (6.30)	1.44±0.60 (2.73)	*
12	R MB	2.72±1.67 (6.90)	0.93±0.48 (1.90)	*
13	L MB	2.84±1.70 (6.14)	1.01±0.62 (2.93)	*
14	pineal gland	2.53±1.39 (5.70)	2.01±1.24 (6.16)	
15	R LV at AC	4.44±1.84 (7.90)	2.70±1.59 (7.85)	*
16	L LV at AC	4.50±1.95 (8.40)	2.11±1.72 (7.92)	*
17	R LV at PC	4.81±2.54 (10.07)	2.96±2.42 (9.46)	*
18	L LV at PC	4.80±2.64 (10.34)	3.01±2.22 (8.13)	*
19	genu of CC	3.73±1.82 (7.88)	1.56±0.76 (3.32)	*
20	splenium	2.96±1.88 (7.57)	0.97±0.60 (2.93)	*
21	R AL temporal horn	3.79±1.71 (7.50)	1.70±1.09 (5.23)	*
22	L AL temporal horn	3.62±1.45 (6.98)	1.67±0.98 (4.31)	*
23	R superior AM temporal horn	3.34±1.63 (7.25)	1.93±1.34 (6.85)	*
24	L superior AM temporal horn	3.44±1.80 (8.20)	1.67±1.25 (5.80)	*
25	R inferior AM temporal horn	4.02±1.97 (8.32)	2.41±1.16 (5.61)	*
26	L inferior AM temporal horn	4.13±1.70 (8.20)	2.21±1.09 (4.84)	*
27	R indusium griseum origin	3.36±2.07 (8.46)	2.06±1.49 (6.40)	*
28	L indusium griseum origin	3.60±1.68 (8.83)	2.05±1.37 (5.00)	*
29	R ventral occipital horn	5.86±6.32 (36.26)	3.44±5.77 (32.78)	*
30	L ventral occipital horn	6.99±6.72 (33.74)	4.51±6.28 (29.76)	*
31	R olfactory sulcal fundus	2.83±1.36 (7.50)	1.37±0.95 (3.44)	*
32	L olfactory sulcal fundus	2.94±1.28 (6.49)	1.57±0.84 (3.41)	*



Subject level analysis of lin versus nlin

Revealed 3 subjects where mean AFRE was not statistically different. However, individual afids demonstrated high AFRE.

One subject appeared to be well registered with linear registration alone. The other two had extreme registration errors (over 8 mm AFRE).

subject	AFRE_lin	AFRE_nlin	AFRE_qval_significant
OAS1_0010	4.44±2.06 (11.19)	1.82±1.25 (5.61)	*
OAS1_0086	3.19±1.41 (6.40)	1.33±1.14 (5.66)	*
OAS1_0101	3.10±2.22 (8.83)	2.46±2.14 (8.36)	
OAS1_0109	4.86±8.12 (36.26)	3.89±7.34 (32.78)	
OAS1_0114	3.31±2.03 (8.32)	1.52±1.21 (5.88)	*
OAS1_0117	4.08±2.15 (9.76)	1.74±1.81 (10.12)	*
OAS1_0145	2.33±1.69 (7.57)	1.27±1.45 (6.85)	*
OAS1_0177	2.84±1.78 (7.06)	1.54±0.82 (2.83)	*
OAS1_0180	4.08±2.20 (10.13)	2.52±1.69 (6.45)	*
OAS1_0188	3.35±1.80 (9.08)	1.65±1.21 (5.08)	*
OAS1_0200	2.56±1.45 (7.88)	1.47±0.96 (4.84)	*
OAS1_0203	3.78±3.89 (23.96)	2.46±3.89 (22.40)	*
OAS1_0216	2.19±1.61 (7.58)	1.73±1.02 (4.48)	
OAS1_0239	2.89±2.03 (11.68)	1.56±1.63 (8.55)	*
OAS1_0249	3.34±1.65 (8.53)	1.63±1.08 (4.66)	*
OAS1_0255	3.48±1.77 (6.68)	1.29±0.75 (3.16)	*
OAS1_0256	4.16±2.00 (7.90)	1.52±0.97 (3.56)	*
OAS1_0263	3.97±2.36 (10.34)	1.29±0.96 (3.96)	*
OAS1_0266	3.67±1.18 (7.50)	1.60±1.22 (6.16)	*
OAS1_0274	2.90±1.87 (7.73)	1.99±2.34 (8.13)	*
OAS1_0284	3.90±2.59 (13.41)	1.84±1.85 (8.39)	*
OAS1_0303	2.70±1.23 (5.41)	1.47±0.85 (4.03)	*
OAS1_0343	3.32±1.69 (7.95)	2.43±1.95 (9.46)	*
OAS1_0345	2.31±1.30 (6.16)	1.57±1.10 (4.11)	*
OAS1_0357	2.58±1.61 (7.43)	1.47±1.35 (5.30)	*
OAS1_0365	4.18±2.07 (9.61)	1.65±1.35 (6.50)	*
OAS1_0371	2.64±1.31 (6.92)	1.33±0.82 (3.81)	*
OAS1_0395	3.27±1.96 (11.14)	1.68±1.28 (6.68)	*
OAS1_0398	3.85±3.04 (12.40)	1.81±1.80 (9.09)	*
OAS1_0456	4.64±2.73 (12.72)	2.42±2.01 (9.59)	*

Finding Outlier Misregistrations

Here we identify all AFID points across subjects above some minimum threshold of AFRE error (arbitrarily set to 5 mm for notebook presentation purposes).

	fid	subject	name	description	AFRE
212	8	OAS1_0180	8	R inferior LMS	5.411179
271	10	OAS1_0456	10	culmen	9.585257
277	10	OAS1_0239	10	culmen	8.550554
278	10	OAS1_0117	10	culmen	10.118020
289	10	OAS1_0101	10	culmen	8.359801
402	14	OAS1_0266	14	pineal gland	6.158929
435	15	OAS1_0274	15	R LV at AC	7.848187
451	16	OAS1_0456	16	L LV at AC	5.677177
463	16	OAS1_0274	16	L LV at AC	7.922394
471	16	OAS1_0101	16	L LV at AC	5.436124
485	17	OAS1_0101	17	R LV at PC	5.918516
486	17	OAS1_0180	17	R LV at PC	6.450083
490	17	OAS1_0395	17	R LV at PC	6.676601
491	17	OAS1_0274	17	R LV at PC	7.440260
505	17	OAS1_0188	17	R LV at PC	5.084890
506	17	OAS1_0343	17	R LV at PC	9.463697
507	17	OAS1_0284	17	R LV at PC	5.832009
518	18	OAS1_0274	18	L LV at PC	8.125230
520	18	OAS1_0343	18	L LV at PC	6.852881
527	18	OAS1_0456	18	L LV at PC	5.597730
528	18	OAS1_0180	18	L LV at PC	5.111037
534	18	OAS1_0101	18	L LV at PC	7.257325
535	18	OAS1_0365	18	L LV at PC	6.501676
537	18	OAS1_0284	18	L LV at PC	5.089356
538	18	OAS1_0010	18	L LV at PC	5.331059
621	21	OAS1_0180	21	R AL temporal horn	5.232758
667	23	OAS1_0145	23	R superior AM temporal horn	6.847816
674	23	OAS1_0114	23	R superior AM temporal horn	5.875959
718	24	OAS1_0398	24	L superior AM temporal horn	5.141291
719	24	OAS1_0145	24	L superior AM temporal horn	5.803107
737	25	OAS1_0180	25	R inferior AM temporal horn	5.605086
782	27	OAS1_0109	27	R indusium griseum origin	6.403877
851	29	OAS1_0109	29	R ventral occipital horn	32.777012
866	29	OAS1_0284	29	R ventral occipital horn	8.394882
871	30	OAS1_0109	30	L ventral occipital horn	29.762330
872	30	OAS1_0203	30	L ventral occipital horn	22.404038
877	30	OAS1_0010	30	L ventral occipital horn	5.611475
879	30	OAS1_0357	30	L ventral occipital horn	5.304235
886	30	OAS1_0398	30	L ventral occipital horn	9.086490
896	30	OAS1_0086	30	L ventral occipital horn	5.660475

OAS1_0180 OAS1_0456 OAS1_0239 OAS1_0117 OAS1_0101 OAS1_0266 OAS1_0274 OAS1_0395 OAS1_0188 OAS1_0343 OAS1_0284
OAS1_0365 OAS1_0010 OAS1_0145 OAS1_0114 OAS1_0398 OAS1_0109 OAS1_0203 OAS1_0357 OAS1_0086

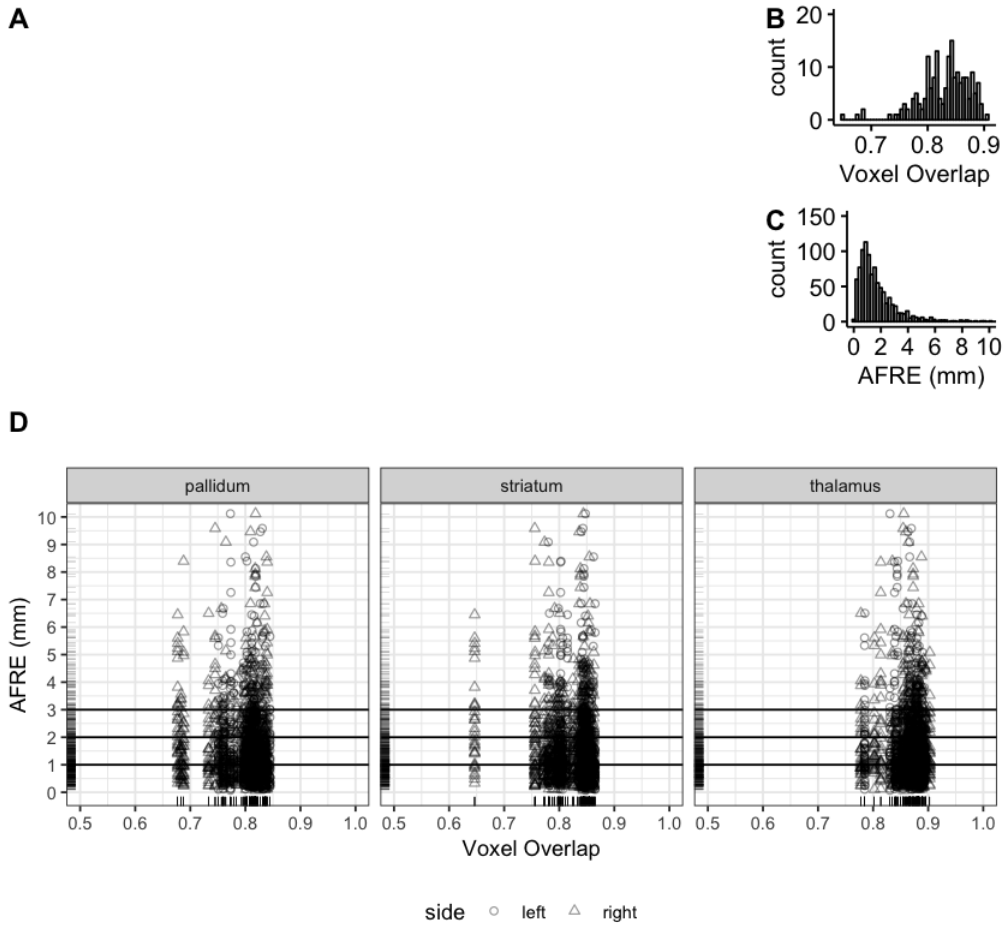
▶ **Levels**:

Investigation of individual OASIS-1 Subject AFIDs (OAS1_0180)

	fid	subject	name	description	AFRE	xfm
15	1	OAS1_0180	1	AC	0.3333971	nlin
33	2	OAS1_0180	2	PC	0.6045653	nlin
62	3	OAS1_0180	3	infracollicular sulcus	0.8774145	nlin
99	4	OAS1_0180	4	PMJ	0.9738354	nlin
125	5	OAS1_0180	5	superior interpeduncular fossa	1.6461190	nlin
177	6	OAS1_0180	6	R superior LMS	0.6837562	nlin
190	7	OAS1_0180	7	L superior LMS	0.4821263	nlin
212	8	OAS1_0180	8	R inferior LMS	5.4111786	nlin
246	9	OAS1_0180	9	L inferior LMS	3.1787138	nlin
293	10	OAS1_0180	10	culmen	3.8186248	nlin
315	11	OAS1_0180	11	intermammillary sulcus	2.3186715	nlin
335	12	OAS1_0180	12	R MB	1.7114213	nlin
365	13	OAS1_0180	13	L MB	2.9269330	nlin
403	14	OAS1_0180	14	pineal gland	2.6319054	nlin
432	15	OAS1_0180	15	R LV at AC	1.7596951	nlin
459	16	OAS1_0180	16	L LV at AC	1.0219584	nlin
486	17	OAS1_0180	17	R LV at PC	6.4500826	nlin
528	18	OAS1_0180	18	L LV at PC	5.1110374	nlin
557	19	OAS1_0180	19	genu of CC	1.4385252	nlin
584	20	OAS1_0180	20	splenium	0.9289616	nlin
621	21	OAS1_0180	21	R AL temporal horn	5.2327578	nlin
641	22	OAS1_0180	22	L AL temporal horn	2.0260472	nlin
663	23	OAS1_0180	23	R superior AM temporal horn	1.4644496	nlin
709	24	OAS1_0180	24	L superior AM temporal horn	1.8499234	nlin
737	25	OAS1_0180	25	R inferior AM temporal horn	5.6050862	nlin
766	26	OAS1_0180	26	L inferior AM temporal horn	2.7429303	nlin
783	27	OAS1_0180	27	R indusium griseum origin	1.3961954	nlin
821	28	OAS1_0180	28	L indusium griseum origin	2.6464879	nlin
863	29	OAS1_0180	29	R ventral occipital horn	3.1210472	nlin
891	30	OAS1_0180	30	L ventral occipital horn	4.8718270	nlin
905	31	OAS1_0180	31	R olfactory sulcal fundus	2.2000853	nlin
933	32	OAS1_0180	32	L olfactory sulcal fundus	3.2115890	nlin

Comparison of AFRE and Voxel Overlap

Evidence for focal misregistrations not captured using voxel overlap measures alone.



Correlation between AFRE and voxel overlap

A weak negative correlation was found between AFRE and standard voxel overlap measures at the global dataset level and for each specific ROI in isolation.

```
        Kendall's rank correlation tau

data:  compare_overlap_AFRE_nlin$jaccard and compare_overlap_AFRE_nlin$AFRE
z = -2.1686, p-value = 0.03011
alternative hypothesis: true tau is not equal to 0
sample estimates:
        tau
-0.01911451

        Kendall's rank correlation tau

data:  compare_overlap_AFRE_nlin$kappa and compare_overlap_AFRE_nlin$AFRE
z = -2.1686, p-value = 0.03011
alternative hypothesis: true tau is not equal to 0
sample estimates:
        tau
-0.01911451

        Kendall's rank correlation tau

data:  compare_overlap_AFRE_nlin$jaccard and compare_overlap_AFRE_nlin$kappa
z = 113.2, p-value < 2.2e-16
alternative hypothesis: true tau is not equal to 0
sample estimates:
tau
  1
```

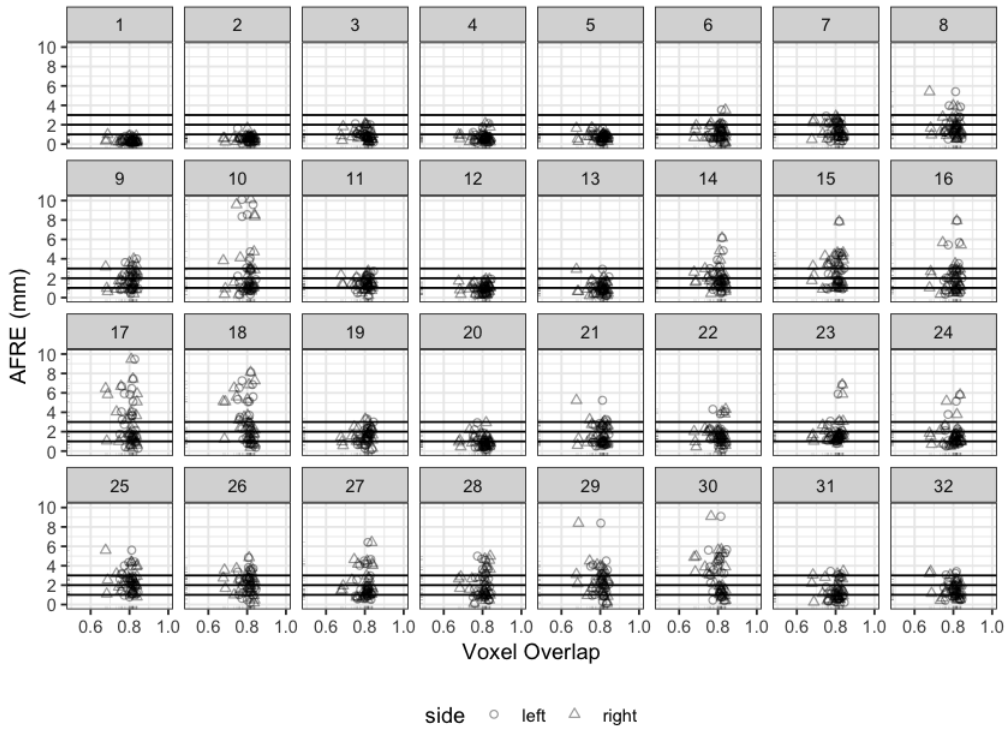
roi	side	AFRE_jaccard	AFRE_jaccard_pval	AFRE_kappa	AFRE_kappa_pval	AFRE_jaccard_pval_adjusted	AFRE_jaccard_pval_significant	AFRE_kappa_pv
pallidum	left	-0.021863046	0.31813186	-0.021863046	0.31813186	0.3817582	FALSE	0.3817582
pallidum	right	-0.045837311	0.03634823	-0.045837311	0.03634823	0.1090447	FALSE	0.1090447
striatum	left	-0.034786535	0.11219299	-0.034786535	0.11219299	0.2243860	FALSE	0.2243860
striatum	right	-0.049644573	0.02339900	-0.049644573	0.02339900	0.1090447	FALSE	0.1090447
thalamus	left	0.006607498	0.76287336	0.006607498	0.76287336	0.7628734	FALSE	0.7628734
thalamus	right	-0.029857412	0.17277515	-0.029857412	0.17277515	0.2591627	FALSE	0.2591627

For each AFID and ROI

No correlation between voxel overlap measures and individual AFID AFREs were identified. However, plotting of voxel overlap against individual AFREs demonstrate the added sensitivity to misregistration when looking at individual AFID plots along the y-axis.

```
'Number of significant correlations (individual AFIDs vs voxel overlap): 0/192 (0.0%)'
```

Pallidum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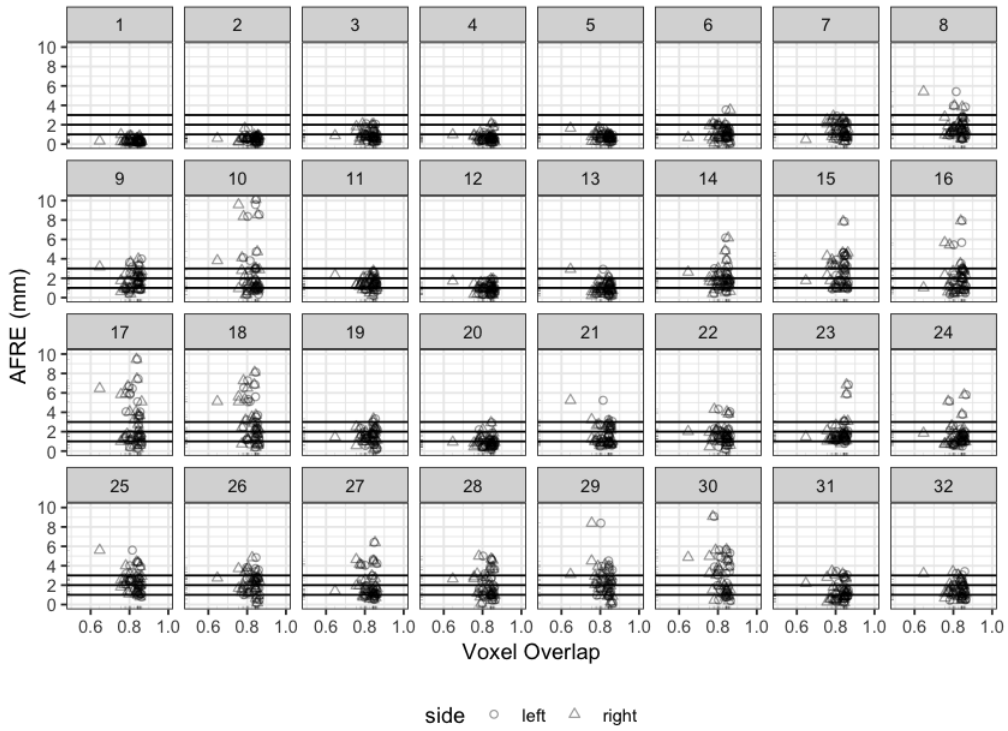
AFRE (mm)
Voxel Overlap
side
left
right

Striatum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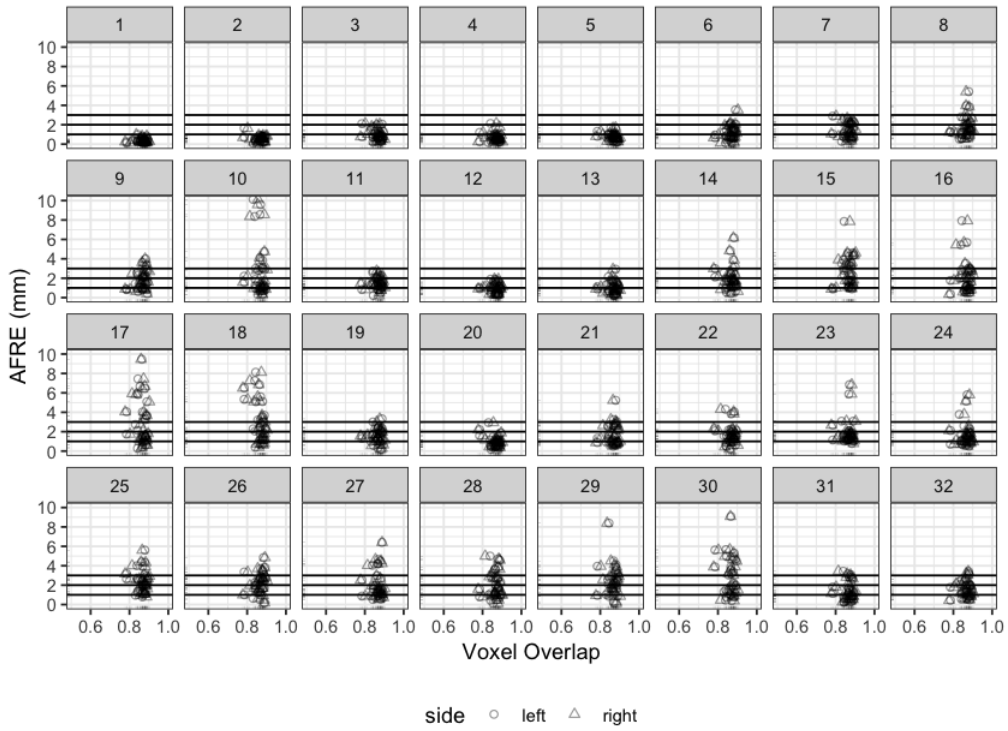
AFRE (mm)
Voxel Overlap
side
left
right

Thalamus



AFLE versus AFRE

In this section, we examine whether AFLE and AFRE are correlated and establish a baseline for when AFRE should be considered beyond placement-related (AFLE) error. The first vertical line is the mean AFLE for OASIS-1 subjects. Second is 1 s.d., third is 2 s.d.

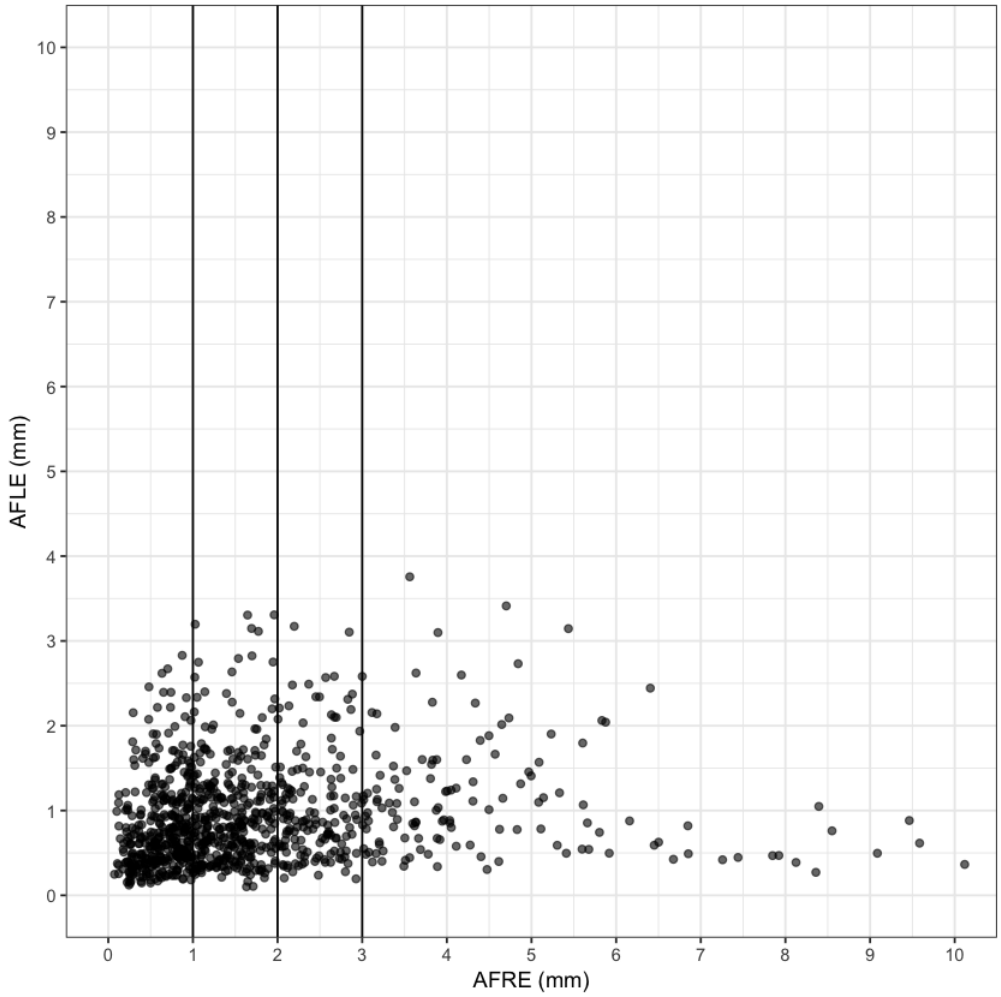
A positive correlation between AFLE and AFRE was found to be statistically significant although the actual effect size of the correlation was small.

'Num Outlier AFIDs (> 2 s.d. above mean AFLE): 135/960 (14.06%)'

'Num Unique Outlier AFIDs (> 2 s.d. above mean AFLE): 22/32 (68.75%)'

```
        Kendall's rank correlation tau

data:  AFLE_vs_AFRE$AFRE and AFLE_vs_AFRE$mean_AFLE
z = 6.9796, p-value = 2.959e-12
alternative hypothesis: true tau is not equal to 0
sample estimates:
      tau
0.1504519
```



Secondary Analyses

We evaluated whether there was any evidence of an effect of demographics (e.g. age of the participants being registered) on AFRE. Age resulted in a global AFRE change of 0.0075 mm/year (i.e. a small but statistically significant effect). No specific AFIDs were found to contribute to this age-related AFRE change after multiple comparisons correction.

(Intercept)	2.1635	0.0000
age	0.0075	0.0191

fid	(Intercept)	pval_(Intercept)	age	pval_age	pval_age_adjusted	pval_age_significant
1	1.15	0.03	0.00	0.83	0.86	FALSE
2	1.22	0.01	0.00	0.96	0.96	FALSE
3	1.96	0.00	-0.01	0.42	0.75	FALSE
4	0.72	0.23	0.01	0.13	0.55	FALSE
5	1.77	0.00	0.00	0.66	0.83	FALSE
6	1.74	0.00	0.00	0.78	0.83	FALSE
7	1.03	0.01	0.01	0.05	0.43	FALSE
8	0.62	0.25	0.03	0.01	0.16	FALSE
9	1.54	0.00	0.01	0.20	0.55	FALSE
10	6.53	0.00	-0.05	0.02	0.32	FALSE
11	1.41	0.03	0.01	0.23	0.56	FALSE
12	0.90	0.18	0.02	0.15	0.55	FALSE
13	0.75	0.28	0.02	0.08	0.50	FALSE
14	2.07	0.00	0.00	0.72	0.83	FALSE
15	2.72	0.00	0.01	0.30	0.64	FALSE
16	2.12	0.03	0.02	0.20	0.55	FALSE
17	2.32	0.05	0.03	0.16	0.55	FALSE
18	1.65	0.14	0.04	0.04	0.40	FALSE
19	2.30	0.01	0.01	0.65	0.83	FALSE
20	2.34	0.00	-0.01	0.61	0.83	FALSE
21	2.52	0.00	0.00	0.77	0.83	FALSE
22	2.87	0.00	0.00	0.74	0.83	FALSE
23	3.42	0.00	-0.01	0.26	0.60	FALSE
24	2.88	0.00	-0.01	0.67	0.83	FALSE
25	2.51	0.00	0.01	0.36	0.71	FALSE
26	2.21	0.01	0.02	0.19	0.55	FALSE
27	3.19	0.00	-0.01	0.56	0.83	FALSE
28	3.20	0.00	-0.01	0.61	0.83	FALSE
29	2.43	0.38	0.04	0.40	0.75	FALSE
30	2.19	0.45	0.06	0.21	0.55	FALSE
31	2.48	0.00	-0.01	0.52	0.83	FALSE
32	2.47	0.00	0.00	0.70	0.83	FALSE

```
R version 3.5.1 (2018-07-02)
Platform: x86_64-apple-darwin14.5.0 (64-bit)
Running under: macOS High Sierra 10.13.2

Matrix products: default
BLAS: /System/Library/Frameworks/Accelerate.framework/Versions/A/Frameworks/vecLib.framework/Versions/A/libBLAS.dylib
LAPACK: /System/Library/Frameworks/Accelerate.framework/Versions/A/Frameworks/vecLib.framework/Versions/A/libLAPACK.dylib

locale:
[1] en_CA.UTF-8/en_CA.UTF-8/en_CA.UTF-8/C/en_CA.UTF-8/en_CA.UTF-8

attached base packages:
[1] stats     graphics  grDevices utils     datasets  methods   base

other attached packages:
[1] bindrcpp_0.2.2 ggpubr_0.1.8   magrittr_1.5   ggplot2_3.0.0  reshape2_1.4.3
[6] digest_0.6.16  dplyr_0.7.6    plyr_1.8.4

loaded via a namespace (and not attached):
 [1] Rcpp_0.12.17     pillar_1.3.0     compiler_3.5.1   bindr_0.1.1
 [5] base64enc_0.1-3  tools_3.5.1      uuid_0.1-2       jsonlite_1.5
 [9] evaluate_0.11    tibble_1.4.2     gtable_0.2.0     pkgconfig_2.0.2
[13] rlang_0.2.1      IRdisplay_0.5.0  IRkernel_0.8.12  repr_0.15.0
[17] withr_2.1.2      stringr_1.3.1    cowplot_0.9.3    grid_3.5.1
[21] tidyselect_0.2.4 glue_1.3.0       R6_2.2.2         pbdZMQ_0.3-3
[25] purrr_0.2.5      scales_1.0.0     htmltools_0.3.6  assertthat_0.2.0
[29] colorspace_1.3-2 labeling_0.3     stringi_1.2.4    lazyeval_0.2.1
[33] munsell_0.5.0    crayon_1.3.4
```