Optimization of Preprocessing Strategies in Positron Emission Tomography (PET): A [^{11}C]DASB PET Study

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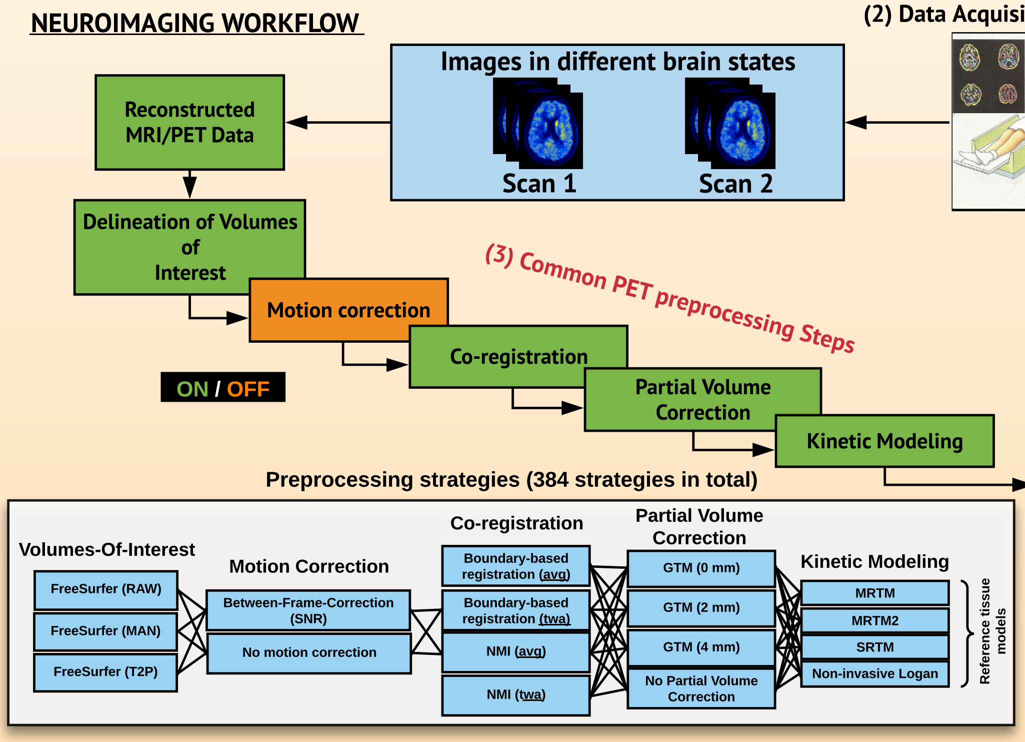
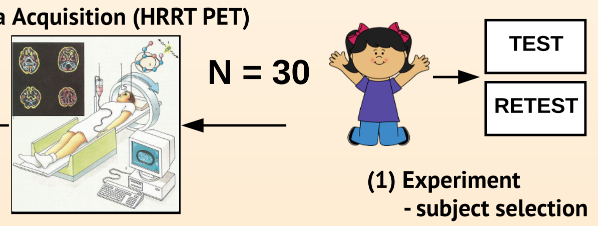
Motivation

- **Seemingly small changes in preprocessing strategy**, within a **neuroimaging workflow,** may have **impact on PET studies, potentially biasing the biological conclusions.**
- To **evaluate the impact of various preprocessing strategies**, we examined **384 strategies** in 30 subjects who were scanned twice with the **serotonin transporter (5-HTT) radioligand [^{11}C]DASB**. The impact was quantitatively compared and **evaluated using 6 performance metrics.**

Significance Statement

- **Maximally powered neuroimaging results** can **be obtained** by making **appropriate preprocessing choices** depending on the **neuroscientific question.**
- **Given that *no* apriori hypothesis exists**, we recommend researchers to use the FIX pipeline (Table 1).
- **Given that *a* specific hypothesis exists** (e.g. putamen), we recommend researchers to use Table 1 as guideline.





1. **Global Reproducibiliity Metric (FIX)**

$$gSNR_{i,k} = \sqrt{\frac{(1+R_{i,k})-(1-R_{i,k})}{(1-R_{i,k})}}$$, R = Pearson's correlation

2. **Test-retest bias**

$$bias_{i,j,k} = 100 \times \left(\frac{retest_{i,j,k} - test_{i,j,k}}{test_{i,j,k}}\right)$$

3. **Within-subject variability (WSV)**

$$WSV_{j,k} = 100 \times \left(\frac{std(d_{i,j,k} - \bar{d}_{j,k})}{mean((test_{i,j,k} + retest_{i,j,k})/2)}\right)$$

4. **Between-subject variability (BSV)**

$$BSV_{j,k} = 100 \times \left(\frac{\sigma_{j,k,test}}{\mu_{j,k,test}}\right)$$

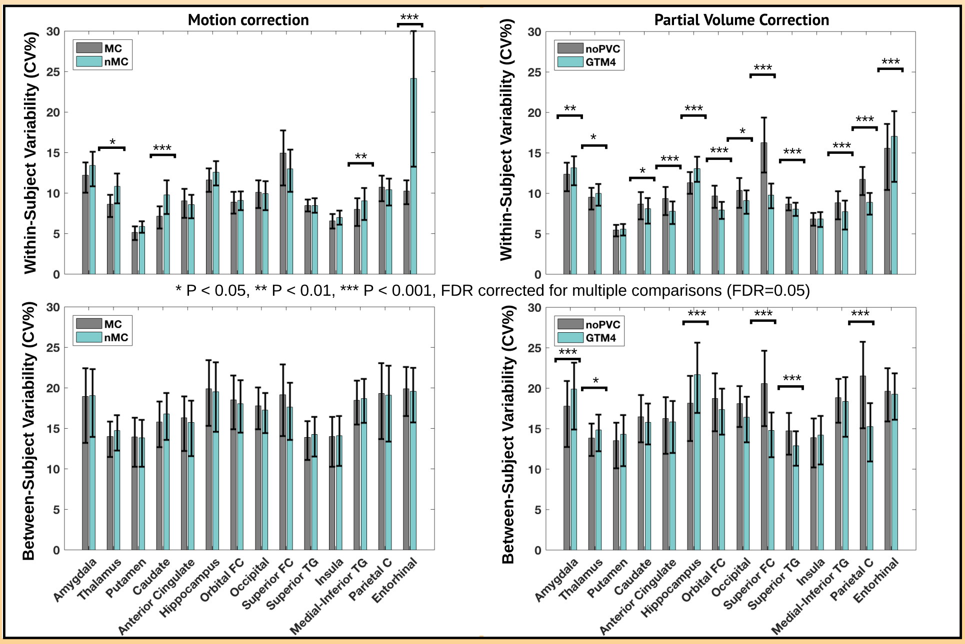
5. **Intraclass-Correlation Coefficient (ICC)**

$$ICC_{j,k} = \frac{MSBS_{j,k} - MSE_{j,k}}{MSBS_{j,k} + (q-1)MSE_{j,k}}$$

6. **Power Analysis**

$$\hat{n}_{j,k} = \left(\frac{1.96 \times \sigma_{j,k,test}}{E_{j,k}}\right)^2$$, E = Effect of either 5% or 10%

(4) Performance Metrics to measure pipeline performance for subject *i*, region *j*, and pipeline *k*



Preprocessing Strategy Recommendations

	FIX	WSV	BSV	ICC
Amygdala	AAAAB	CBBCB	BAAAD	ABACB
Thalamus	AAAAB	BAAAA	ABBAD	BABDA
Putamen	AAAAB	CAAAA	CADDA	AABDA
Caudate	AAAAB	CAADB	CADDA	AAADB
Anterior Cingulate	AAAAB	BBADB	ABDDD	CBADB
Hippocampus	AAAAB	BBBAB	ABBAD	CBBCB
Orbital FC	AAAAB	BBBDB	CBDDD	BBADB
Occipital	AAAAB	BABDB	ABDDC	CABDA
Superior FC	AAAAB	ABCDB	ABBDA	CBADC
Superior TG	AAAAB	BBBDB	AABDD	BBABB
Insula	AAAAB	CABBA	BABDD	CBBDB
Medial-Inferior TG	AAAAB	BBBDB	BABDB	CBBDB
Parietal C	AAAAB	ABADA	ABCDB	BBABC
Entorhinal	AAAAB	CABAB	CBBDD	BABDB

Table 1: Overview of optimal pipelines for several brain regions, when optimized by median-rank (FIX), within-subject variability (WSV), between-subject variability (BSV) and intra-class correlation (ICC). 1st letter (Delineation of regions; A=FS-raw, B=FS-man, C=FS-T2p), 2nd letter (Motion Correction (MC); A=MC, B=noMC), 3rd letter (Co-registration; A=BB_{TWA}, B=NMI_{TWA}, C=BB_{AVG}, D=NMI_{AVG}), 4th letter (Partial Volume Correction (PVC); A=noPVC, B=Geometric Transfer Matrix (GTM) 0 mm, C=GTM 2 mm, D=GTM 4 mm), 5th letter (Kinetic modeling; A=MRTM, B=MRTM2, C=SRTM, D=Non-invasive Logan).