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Background

- [¹¹C]UCB-J is a radiotracer targeting the **synaptic vesicle glycoprotein 2A (SV2A)**. Its properties are favourable for quantifying synaptic density in AD.⁽¹⁾
- The gold standard method for PET quantification needs arterial blood sampling, an invasive and constraining procedure.
- **Non-invasive quantification methods** based on the use of a reference region are a non-invasive alternative.
- **DVR** (*distribution volume ratio*) is considered as a reliable method but requires full dynamic PET acquisition.
- **Long acquisition times** are often **difficult for patients** to tolerate, especially if they have neurological disorders.
- **SUVr** (*standardised uptake value ratio*) is calculated at late times and requires shorter acquisition time. This method remains relatively little studied in AD and has rarely been compared to other more established methods such as DVR.
- We compared SUVr with DVR using different reference regions to validate its use in AD.

Materials and Methods

- **Fifty-five patients** with a clinical and biological diagnosis of AD (CSF biomarkers) and **twenty-nine age-matched healthy controls** were included and underwent [¹¹C]UCB-J PET imaging (308.09 ± 36.93 MBq) (*Table 1*). (Three subjects were excluded prior to analysis)
- **Dynamic PET acquisition** lasted **70 min**. **DVR** was calculated using the full dynamic acquisition. **SUVr** was calculated during the **50 to 70 min time window** post-injection.
- Three reference regions were tested (*Figure 2*)⁽²⁻⁵⁾:
 - **Centrum Semiovale** (CS)
 - **Whole cerebellum** (WC)
 - **white matter (2 mm-eroded)** (WM)
- We defined **7 cortical meta-regions of interest (ROI)** for each hemisphere, covering the entire associative cortex.
- **DVR vs SUVr correlations** were evaluated in all participants and 14 ROIs combined.
- We compared the ability of DVR and SUVr to distinguish AD patients from controls with each reference region. Results were expressed as regional effect sizes (Cohen's d).

	AD patients (n=55)	Controls (n=29)
Age (years)	70.0 ± 8.6	68.0 ± 9.6
Sex (M, %)	27 (52%)	12 (41%)
Education (years)	13.6 ± 2.9 *	15.0 ± 2.0
MMSE (/30)	24.1 ± 3.1 *	29.3 ± 0.8
CDR (0 / 0.5 / 1) (% CDR = 0.5)	0 / 49 / 6 (89%) *	29 / 0 / 0 (0%)
CDR-SB (/18)	2.7 ± 1.3 *	0 ± 0

Table 1: Characteristics of participants

* AD patient group significantly different from control groups (p-value < 0.05)

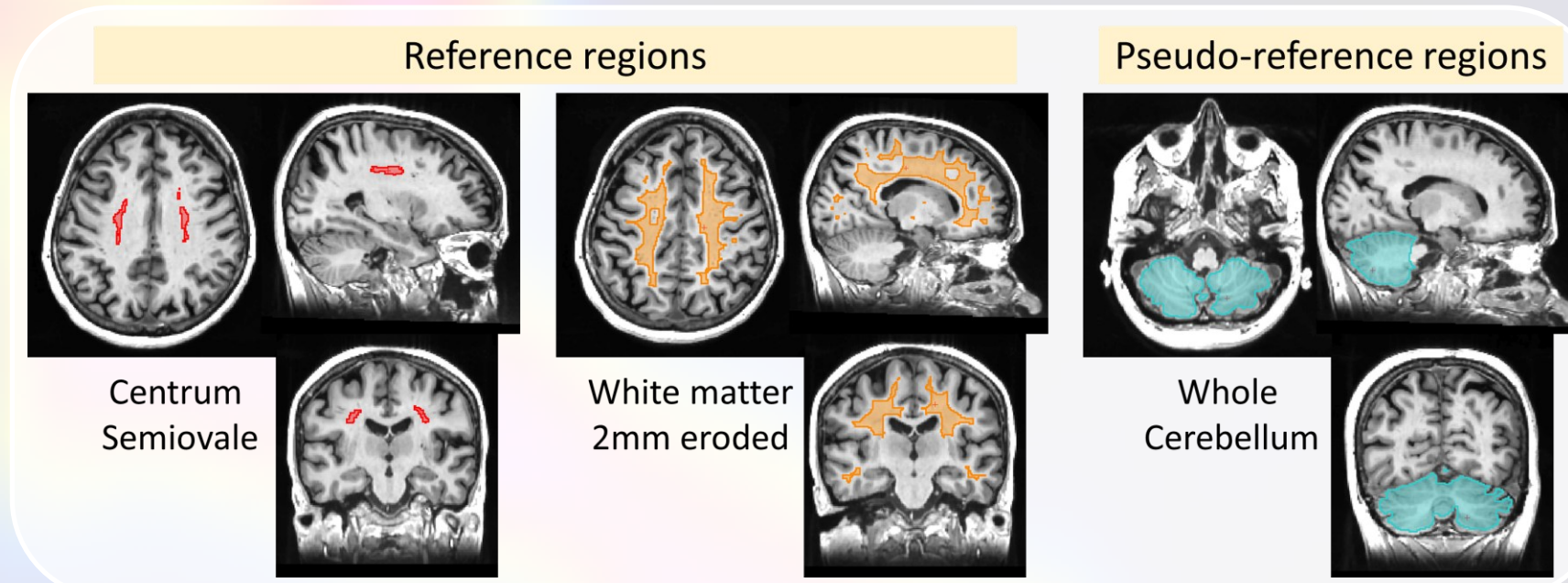


Figure 2: Reference region masks displayed on T1-MRI scan

Results

Correlations of the SUVr_(50-70 min) with the DVR (*Figure 3*)

- We found **strong correlations** between SUVr and DVR values (r > 0.9, p-value < 0.001) with all reference regions.

Ability to distinguish AD patients from controls (*Figure 4*)

- **SUVr and DVR values were significantly lower in AD patients** compared to controls whatever the reference regions used. The differences were **particularly pronounced** in the lateral parietal, medial parietal, and lateral temporal cortices.
- **Effect sizes (Cohen's d) with DVR were slightly higher than with SUVr** when using WC or WM as the reference region.
- **The differences were slightly stronger with WC than with WM** (for both the DVR and the SUVr)
- **The differences were less pronounced when the CS was used as the reference region.**

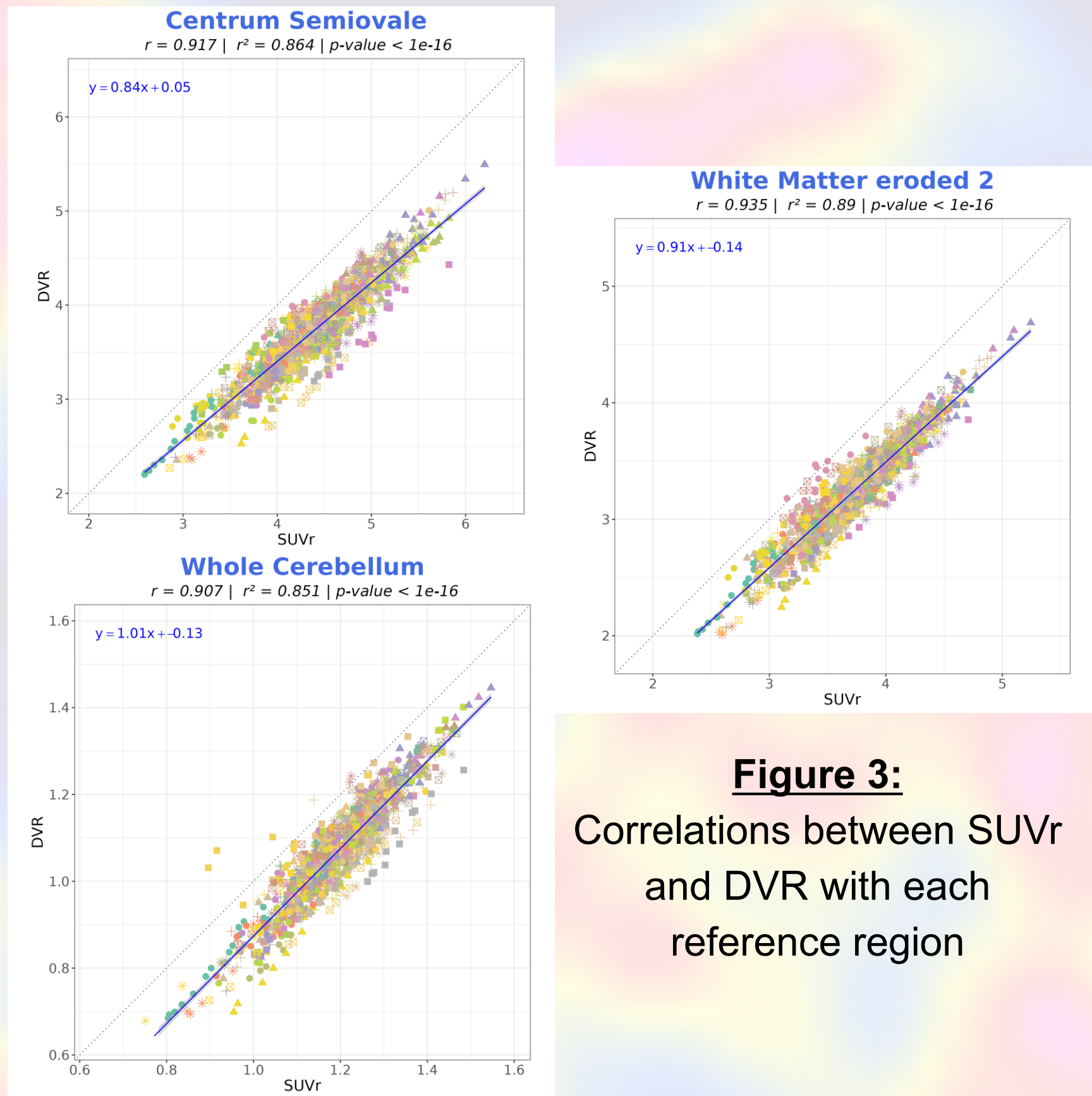


Figure 3: Correlations between SUVr and DVR with each reference region

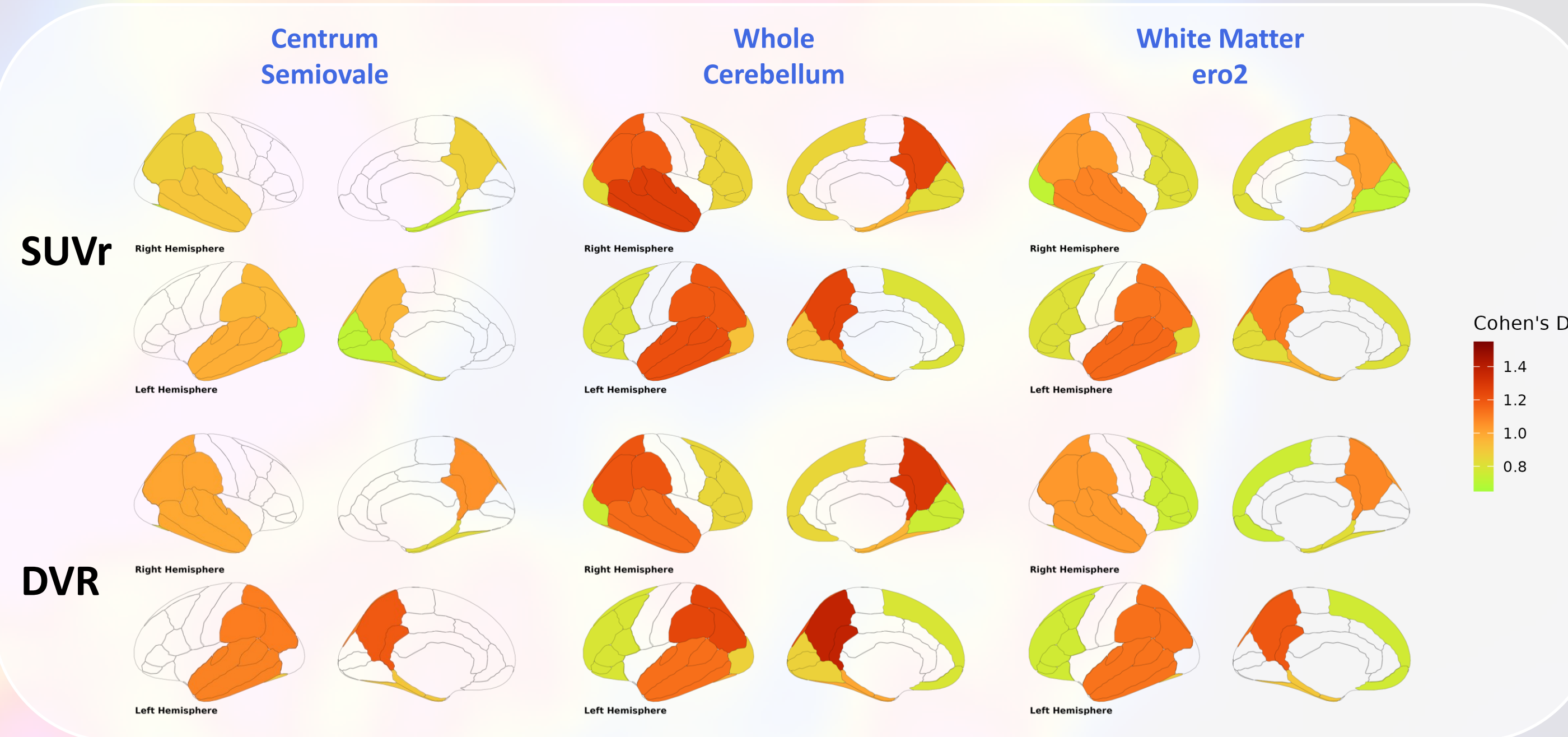


Figure 4: Effect size expressed by Cohen's D when the comparison between AD patients and controls is significant in SUVr and DVR, as a function of the reference region (p<0.05 after Bonferroni correction for multiple comparisons)

Conclusion

- ⇒ Our results suggest that the **SUVr_(50-70 min)** is a **valid method for UCB-J quantification in AD**
- ⇒ **The Whole Cerebellum** appears to be the **most appropriate reference region to quantify [¹¹C]UCB-J binding**.
- ⇒ The **2 mm-eroded white matter** has characteristics similar to those of the WC, with advantages over the CS. Its usage **could be considered when a true reference region is required**.

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