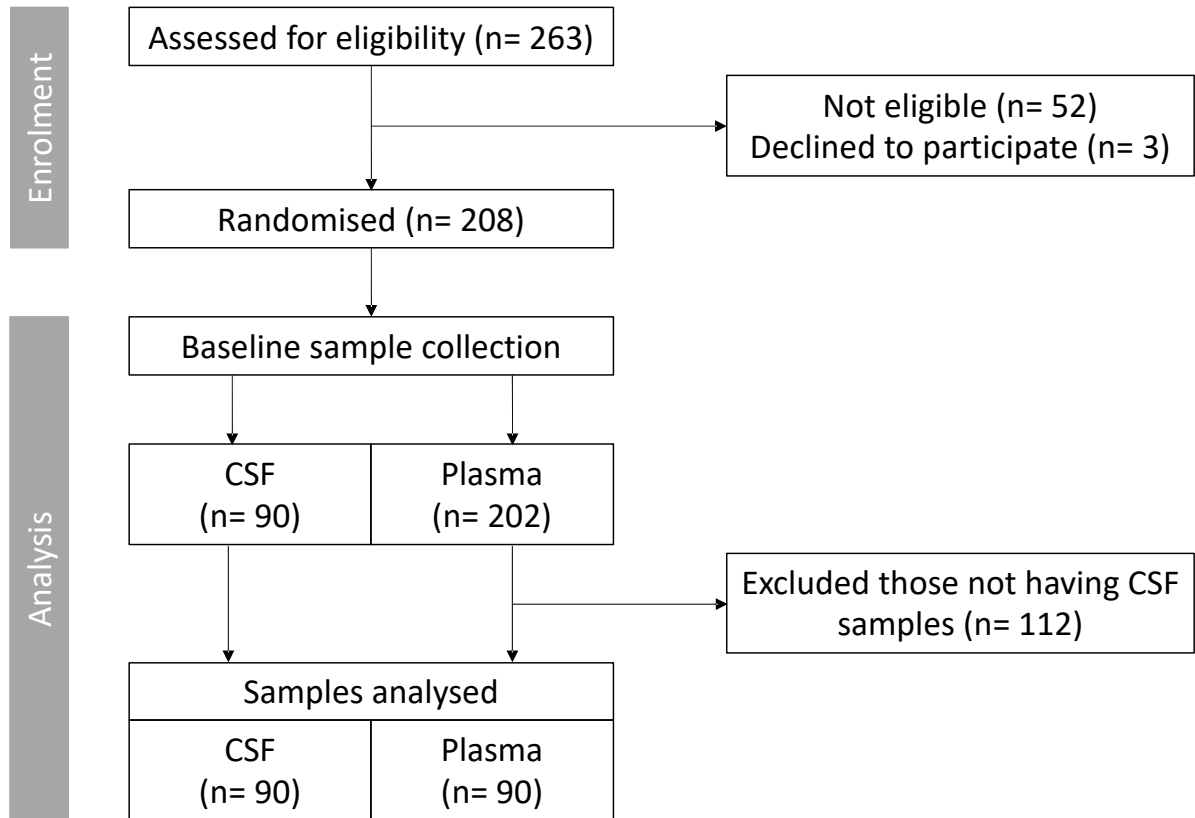


**Identification and quantification of (poly)phenol and
methylxanthine metabolites in human cerebral spinal fluid:
evidence of their ability to cross the BBB.**

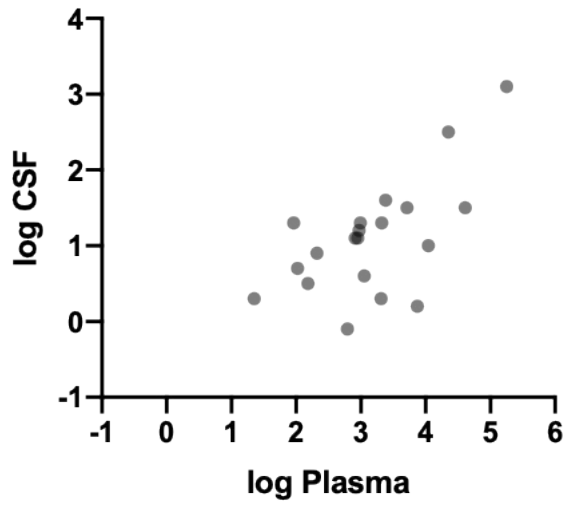
Melanie Le Sayec¹, Diogo Carregosa², Khadija Khalifa³, Chiara de
Lucia⁴, Dag Aarsland⁴, Cláudia N Santos² and Ana Rodriguez-Mateos^{1*}.

Supplementary Figures

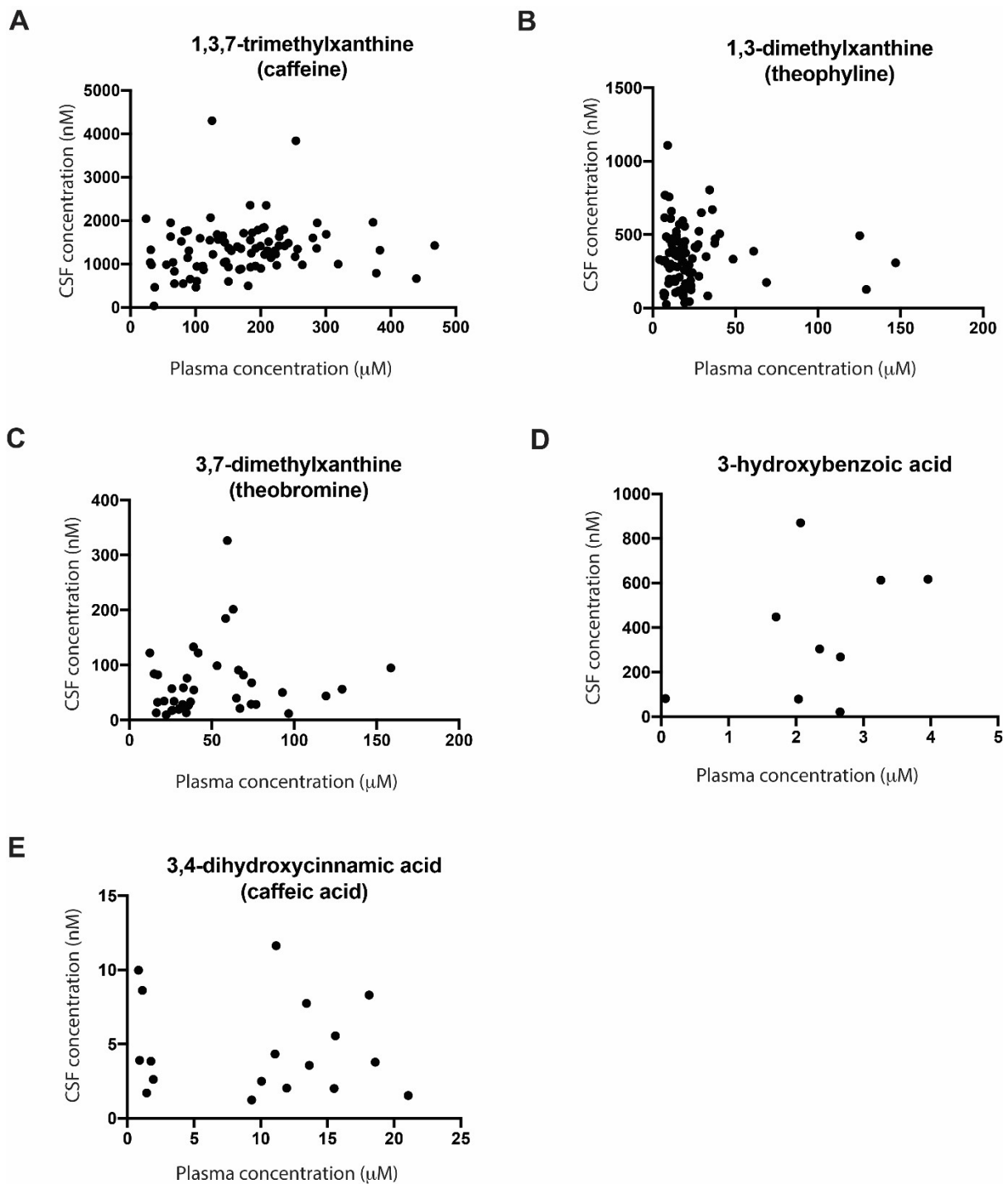
Supplementary Figure S1. Flow Chart study



Supplementary Figure S2. Correlation between the concentrations of the 20 metabolites quantified in both CSF and plasma. Pearson correlation coefficient = 0.63, $p = 0.003$, 95%CI= 0.265-0.840



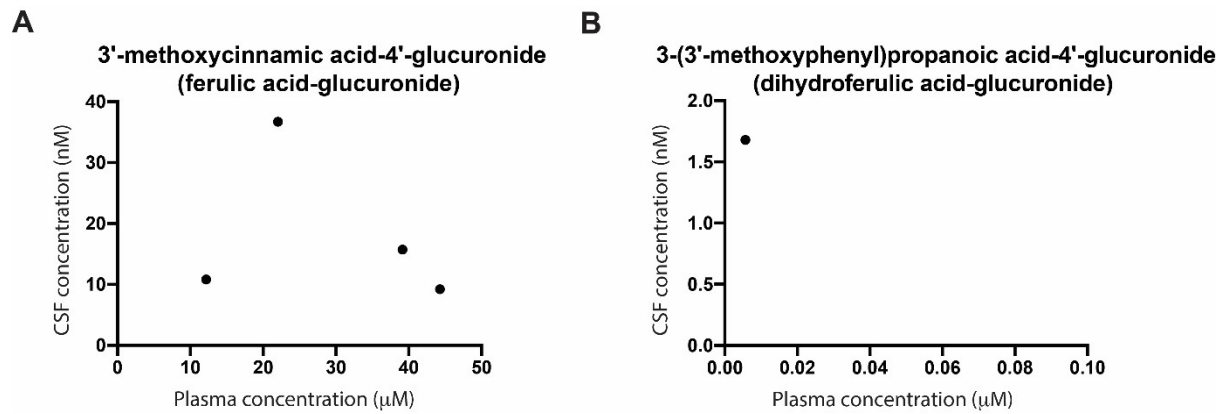
Supplementary Figure S3. Plasma and CSF concentrations show high degree of variability amongst volunteers for: (A) 1,3,5-trimethylxanthine, (B) 1,3-dimethylxanthine, (C) 3,7-dimethylxanthine, (D) 3-hydroxybenzoic acid, (E) 3',4'-dihydroxycinnamic acid.



Supplementary Figure S4. Plasma and CSF concentrations for the molecules

detected on a small number of volunteers. (A) 3'-methoxycinnamic acid-4'-

glucuronide, (B) 3-(3'-methoxyphenyl)propanoic acid-4'-glucuronide.



Supplementary Figure S5. Plasma and CSF concentrations of the molecules that may show some saturation. These molecules showed a coefficient of variation below 10% for CSF concentrations yet have low plasma concentrations. For these reason further studies might be required to fully confirm saturation of CSF concentrations.

(A) quercetin-glucuronide, (B) 4-O-feruoylquinic acid, (C) 7,8-dihydrocoumarin, (D) (-)-epicatechin.

