When biomarkers disagree, what should you believe?

FICTIONAL EXAMPLE | [^{18}F]CAE, SENY, sSENY and all observations below are invented.

01 THE SCIENTIFIC QUESTION

After an intervention, a fictional study reports lower [^{18}F]CAE PET binding, higher plasma sSENY and no detectable memory change. The team asks whether the intervention worked. **Which explanations remain compatible with all three observations?**

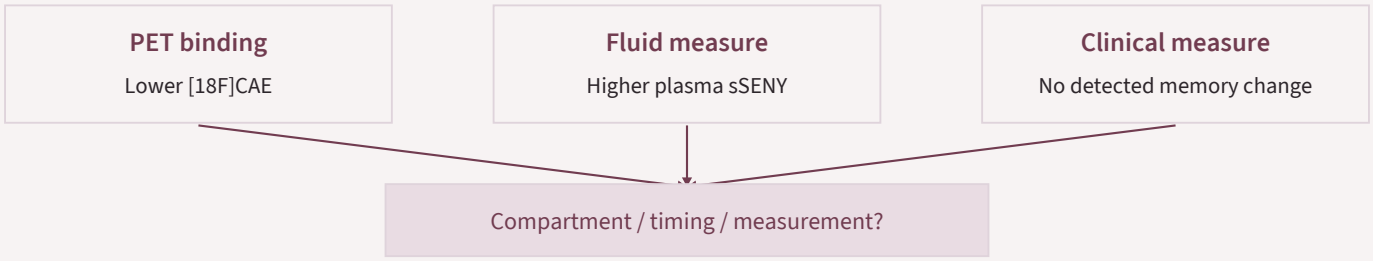


Figure 1. An evidence-review network, not neural connectivity or a measured biological pathway.

02 ASSUMPTIONS TO EXAMINE

PET binding decreases. Consider occupancy, altered SENY availability, delivery and quantification. A binding change does not automatically imply a change in tissue health. [1]
Plasma sSENY increases. This invented soluble fragment could vary with production, release, peripheral sources or clearance. Do not assume blood concentration mirrors brain target availability.
Memory appears stable. No detectable change is not evidence of equivalence. Consider follow-up duration, precision, practice effects and the clinical feature being assessed.

03 IMPLICATIONS FOR INTERPRETATION

Keep different compartments, different timescales and measurement effects in view. A molecular response might precede clinical change, or never produce clinical benefit. A response biomarker is not automatically a surrogate for benefit. [2] Averaging discordant measures into a single success score would need a justified model.

04 RECOMMENDED NEXT STEPS

1. Align sampling times, repeatability estimates and exposure information.
2. Review imaging quality, model stability, sample handling and assay interference.
3. Examine within-person and comparator data, then select an independent measurement that could distinguish competing explanations.

The useful result is a ranked set of explanations and a discriminating next measurement.

SELECTED EVIDENCE | Sources support principles, not the fictional scenarios.

[1] Innis et al. PET binding nomenclature (2007)
[2] FDA-NIH BEST: response biomarkers