# $^{11}$C-glyburide PET imaging unveils the negligible brain penetration of glyburide in humans
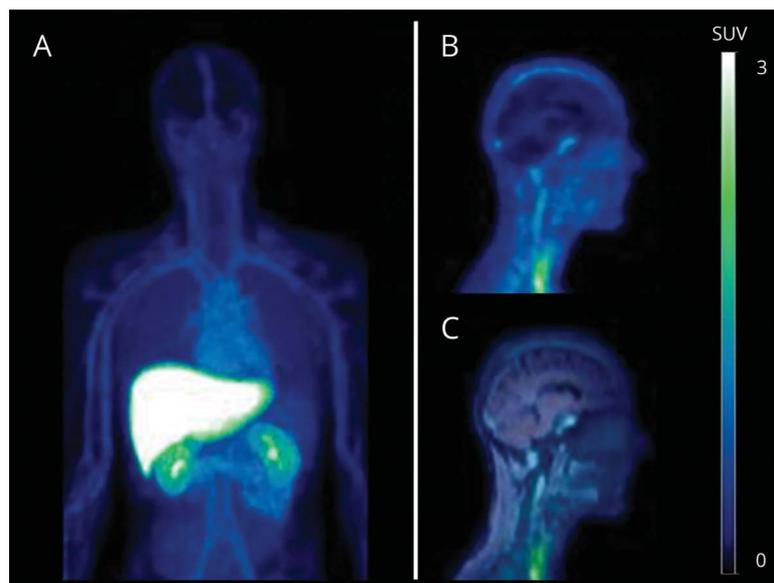
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**Figure** Biodistribution of $^{11}$C-glyburide



Summed PET projection (A), brain PET (B), and PET-MRI fusion (C) images obtained in a 30-year-old healthy man after IV injection of $^{11}$C-glyburide (60 minutes repeated whole-body scans). $^{11}$C-glyburide brain distribution ($V_{T-brain}$ = 0.023 mL.cm$^{-3}$) was estimated using the Logan graphical analysis and the metabolite-corrected arterial input function.

Kimberly et al.[1] reported the beneficial effects of IV glyburide on the clinical outcome of brain edema. We developed the carbon-11 radiolabeled analogue of glyburide to study the body distribution of this compound using PET imaging (figure, A). In a healthy person, the brain distribution of $^{11}$C-glyburide matched the cerebral blood volume, suggesting negligible blood–brain barrier (BBB) penetration (figure, B and C). This clinical observation corroborates preclinical findings suggesting that local changes in BBB structure and function are required for targeted delivery and favorable effects of glyburide to the injured brain tissue while minimizing potential side effects to the healthy brain.[2]

## Study registration

EudraCT 2017-001703-69.

## Study funding

## Disclosure

The authors report no disclosures relevant to the manuscript. Go to Neurology.org/N for full disclosures.

From Imagerie Moléculaire In Vivo (S.M., C.C., F.C., M.B., N.T.), IMIV, Institut des Sciences du Vivant Frédéric Joliot, Direction de la Recherche Fondamentale, CEA, Inserm, CNRS, Paris-Sud University, Université Paris-Saclay, CEA-SHFJ, Orsay; Hôpital Bicêtre (S.M., L.B.), APHP, Le Kremlin Bicêtre; Faculté de Pharmacie (S.M.), Paris-Sud University, Châtenay-Malabry; Department of Pharmacology (L.B.), Paris-Sud University, Faculty of Medicine Paris Sud, INSERM UMR-1178, CESP, Le Kremlin Bicêtre, France.

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## Appendix Authors

| Name | Location | Role | Contribution |
|------|----------|------|--------------|
| Solène Marie, PharmD | CEA/SHFJ | Author | Analyzed the data, wrote the manuscript, study supervision |
| Claude Comtat, PhD | CEA/SHFJ | Author | Major role in the acquisition of data |
| Fabien Caillé, PhD | CEA/SHFJ | Author | Radiotracer production, major role in the acquisition of data |
| Laurent Becquemont, MD, PhD | Paris Sud University | Author | Major role in the acquisition of data, revised the manuscript for intellectual content |
| Michel Bottlaender, MD, PhD | CEA/SHFJ | Author | Designed and conceptualized study, major role in the acquisition of data |
| Nicolas Tournier, PharmD, PhD | CEA/SHFJ | Author | Designed and conceptualized study, drafted the manuscript for intellectual content |

## References

1. Kimberly WT, Bevers MB, von Kummer R, et al. Effect of IV glyburide on adjudicated edema endpoints in the GAMES-RP Trial. Neurology 2018;91:e2163–e2169.
2. Kurland DB, Tosun C, Pampori A, et al. Glibenclamide for the treatment of acute CNS injury. Pharmaceuticals 2013;6:1287–1303.

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