

Neuroplasticity in Diffuse Low-grade Gliomas: Backward Modelling of Brain-tumor Interactions Prior to Diagnosis is Needed to Better Predict Recovery after Treatment

Review Published: 09 January 2025

Volume 25, article number 15, (2025) [Cite this article](#)



[Current Neurology and Neuroscience Reports](#)

[Aims and scope](#)

[Submit manuscript](#)

[Hugues Duffau](#)

115 Accesses [Explore all metrics](#) →

Abstract

Purpose of Review

In low-grade glioma (LGG), besides the patient's neurological status and tumor characteristics on neuroimaging, current treatment guidelines mainly rely on the glioma's genetics at diagnosis to define therapeutic strategy, usually starting with surgical resection. However, this snapshot in time does not take into account the antecedent period of tumor progression and its interactions with the brain before presentation. This article reviews new concepts that pertain to reconstruct the history of previous interplay between the LGG's course and adaptive changes in the connectome within which the glioma is embedded over the years preceding the diagnosis.



Recent Findings

Microscale and macroscale parameters helpful for extrapolating backward in time are considered,

both for the glioma (kinetics, migration vs. proliferation profile, metabolism with possible intratumoral heterogeneity, relationships with surrounding cerebral pathways) and for patterns of reconfiguration within and across neural networks in reaction to the LGG leading to considerable interindividual cerebral variability. Modelling these continuous variations at the time of LGG diagnosis is a prerequisite to predict recovery from treatment(s).

Summary

It is important to go beyond the biology of the LGG at a given moment of its history, and instead construct a more comprehensive picture of the past and present dynamics of glioma–brain interactions, and their ongoing evolution, as a necessary stage to optimize a personalized management plan by thinking several steps ahead.

 This is a preview of subscription content, [log in via an institution](#)  to check access.

Access this article

[Log in via an institution](#)

[Buy article PDF 39,95 €](#)

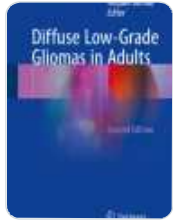
Price includes VAT (Italy)

Instant access to the full article PDF.

Rent this article via [DeepDyve](#) 

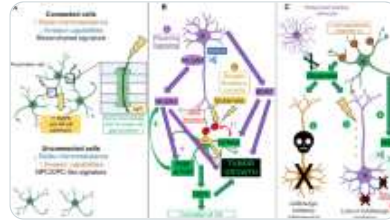
[Institutional subscriptions](#) →

Similar content being viewed by others



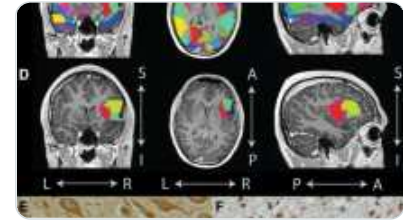
Interactions Between Diffuse Low-Grade Glioma (DLGG), Brain Connectome and Neuroplasticity

Chapter | © 2017



Central nervous system regulation of diffuse glioma growth and invasion: from single unit...

Article | Open access
04 June 2024



Oscillatory brain activity associates with neuroligin-3 expression and predicts progression...

Article | Open access
09 August 2018

Data Availability

No datasets were generated or analysed during the current study.

References

1. Duffau H. Diffuse Low-Grade Gliomas in Adults. 2nd ed. Duffau Ed, 2017. Springer International Publishing: Imprint: Springer; 2017. <https://doi.org/10.1007/978-3-319-55466-2>
2. Ng S, Duffau H. Brain plasticity profiling as a key support to therapeutic decision-making in low-Grade Glioma Oncological Strategies. *Cancers*. 2023;15:3698. <https://doi.org/10.3390/cancers15143698>.

[Article](#) [PubMed](#) [PubMed Central](#) [Google Scholar](#)

3. Ng S, Rigau V, Moritz-Gasser S, Gozé C, Darlix A, Herbet G, Duffau H. Long-term autonomy, professional activities, cognition, and overall survival after awake functional-based surgery in patients with IDH-mutant grade 2 gliomas: a retrospective cohort study. *Lancet RH Europe*, in press. This is the first experience ever reported with a median OS beyond 20 years and with a long-term preservation of an active life in a large cohort of 600 patients with IDH-mutated grade 2 gliomas.
4. Weller M, van den Bent M, Preusser M, le Rhun E, Tonn JC, Minniti G, et al. EANO guidelines on the diagnosis and treatment of diffuse gliomas of adulthood. *Nat Rev Clin Oncol*. 2021;18:170–

86. <https://doi.org/10.1038/s41571-020-00447-z>.

[Article](#) [PubMed](#) [Google Scholar](#)

5. Louis DN, Perry A, Wesseling P, Brat DJ, Cree IA, Figarella-Branger D, et al. The 2021 WHO classification of tumors of the Central Nervous System: a Summary. *Neurooncology*. 2021;23:1231–51. <https://doi.org/10.1093/neuonc/noab106>.

[Article](#) [CAS](#) [Google Scholar](#)

6. European Low-Grade Glioma Network. Evidence-based management of adult patients with diffuse glioma. *Lancet Oncol*. 2017;18:e429. doi: 10.1016/S1470-2045(17)30510-7. Epub 2017 Jul 26. PMID: 28759376.

7. Chanbour H, Chotai S. Review of intraoperative adjuncts for maximal safe resection of Gliomas and its impact on outcomes. *Cancers (Basel)*. 2022;14:5705. <https://doi.org/10.3390/cancers14225705>.

[Article](#) [CAS](#) [PubMed](#) [Google Scholar](#)

8. Jiang S, Chai H, Tang Q. Advances in the intraoperative delineation of malignant glioma margin. *Front Oncol*. 2023;13:1114450. <https://doi.org/10.3389/fonc.2023.1114450>. eCollection 2023.

9. Bin-Alamer O, Abou-Al-Shaar H, Gersey ZC, Huq S, Kallos JA, McCarthy DJ, et al. Intraoperative Imaging and Optical Visualization Techniques for Brain Tumor Resection: a narrative review. *Cancers (Basel)*. 2023;15:4890. <https://doi.org/10.3390/cancers15194890>.

[Article](#) [PubMed](#) [Google Scholar](#)

10. Duffau H, Filippi M. Moving towards a connectomic view of neuro-oncology. *Lancet Neurol*. 2024;23:655–56. [https://doi.org/10.1016/S1474-4422\(23\)00291-0](https://doi.org/10.1016/S1474-4422(23)00291-0).

[Article](#) [PubMed](#) [Google Scholar](#)

11. Capelle L, Fontaine D, Mandonnet E, Taillandier L, Golmard JL, Bauchet L, et al. Spontaneous and therapeutic prognostic factors in adult hemispheric World Health Organization Grade II gliomas: a series of 1097 cases. *J Neurosurg*. 2013;118:1157–68. <https://doi.org/10.3171/2013.11.JNS12107>.

doi.org/10.3171/2013.1.JNS121.

[Article](#) [PubMed](#) [Google Scholar](#)

12. Hervey-Jumper SL, Zhang Y, Phillips JJ, Morshed RA, Young JS, McCoy L, et al. Interactive effects of Molecular, Therapeutic, and patient factors on outcome of diffuse low-Grade Glioma. *J Clin Oncol*. 2023;41:2029–42. <https://doi.org/10.1200/JCO.21.02929>.

[Article](#) [CAS](#) [PubMed](#) [PubMed Central](#) [Google Scholar](#)

13. Verdier M, Deverdun J, de Champfleury NM, Duffau H, Lam P, et al. Evaluation of a nnu-net type automated clinical volumetric tumor segmentation tool for diffuse low-grade glioma follow-up. *J Neuroradiol*. 2024;51:16–23. <https://doi.org/10.1016/j.neurad.2023.05.008>.

[Article](#) [PubMed](#) [Google Scholar](#)

14. Chaichana KL, McGirt MJ, Laterra J, Olivi A, Quiñones-Hinojosa A. Recurrence and malignant degeneration after resection of adult hemispheric low-grade gliomas. *J Neurosurg*. 2010;112:10–7. <https://doi.org/10.3171/2008.10.JNS08608>.

[Article](#) [PubMed](#) [Google Scholar](#)

15. Rossi M, Gay L, Ambrogi F, Conti Nibali M, Sciortino T, Puglisi G, et al. Association of supratotal resection with progression-free survival, malignant transformation, and overall survival in lower-grade gliomas. *Neuro Oncol*. 2021;23:812–26. <https://doi.org/10.1093/neuonc/noaa225>.

[Article](#) [PubMed](#) [Google Scholar](#)

16. Duffau H, Pallud J, Mandonnet E. Evidence for the genesis of WHO grade II glioma in an asymptomatic young adult using repeated MRIs. *Acta Neurochir (Wien)*. 2011;153:473–7. <https://doi.org/10.1007/s00701-010-0917-x>.

[Article](#) [PubMed](#) [Google Scholar](#)

17. Gerin C, Pallud J, Grammaticos B, Mandonnet E, Deroulers C, Varlet P, et al. Improving the time-machine: estimating date of birth of grade II gliomas. *Cell Prolif.* 2012;45:76–90. <https://doi.org/10.1111/j.1365-2184.2011.00790.x>.
- [Article](#) [CAS](#) [PubMed](#) [Google Scholar](#)
18. Mandonnet E, Pallud J, Fontaine D, Taillandier L, Bauchet L, Peruzzi P, et al. Inter- and inpatient comparison of WHO grade II glioma kinetics before and after surgical resection. *Neurosurg Rev.* 2010;33(1):91–6. <https://doi.org/10.1007/s10143-009-0229-x>.
- [Article](#) [PubMed](#) [Google Scholar](#)
19. Duffau H. Long-term outcomes after supratotal resection of diffuse low-grade gliomas: a consecutive series with 11-year follow-up. *Acta Neurochir (Wien).* 2016;158:51–8. <https://doi.org/10.1007/s00701-015-2621-32>.
- [Article](#) [PubMed](#) [Google Scholar](#)
20. Pallud J, Blonski M, Mandonnet E, Audureau E, Fontaine D, Sanai N, et al. Velocity of tumor spontaneous expansion predicts long-term outcomes for diffuse low-grade gliomas. *Neuro Oncol.* 2013;15:595–606. <https://doi.org/10.1093/neuonc/nos331>.
- [Article](#) [PubMed](#) [PubMed Central](#) [Google Scholar](#)
21. Gozé C, Blonski M, Le Maistre G, Bauchet L, Dezamis E, Page P, et al. Imaging growth and isocitrate dehydrogenase 1 mutation are independent predictors for diffuse low-grade gliomas. *Neuro Oncol.* 2014;16:1100–9. <https://doi.org/10.1093/neuonc/nou085>.
- [Article](#) [CAS](#) [PubMed](#) [PubMed Central](#) [Google Scholar](#)
22. Mandonnet E. Tumor volume growth as surrogate endpoint in IDH-mt Glioma-Letter. *Clin Cancer Res.* 2024;30:638. <https://doi.org/10.1158/1078-0432.CCR-23-3444>.
- [Article](#) [PubMed](#) [Google Scholar](#)
23. Darlix A, Rigau V, Fraisse J, Gozé C, Fabbro M, Duffau H. Postoperative follow-up for selected diffuse low-grade gliomas with WHO grade III/IV foci. *Neurology.* 2020;94:e830–41. <https://doi.org/10.1212/WNL.0000000000008877>. This is the first study reporting a 5-year survival rate of 95% in patients who did not receive immediate adjuvant treatment after maximal

resection for a low-grade glioma with foci of malignant transformation.

24. Blonski M, Obara T, Brzenczek C, Pouget C, Dillier C, Meyer M, et al. Initial PCV chemotherapy followed by Radiotherapy is Associated with a prolonged response but late neurotoxicity in 20 diffuse low-Grade Glioma patients. *Front Oncol.* 2022;12:827897. <https://doi.org/10.3389/fonc.2022.827897>. The authors showed that in low-grade glioma patients treated by PCV followed by radiotherapy, after a long-term follow-up, substantial neurotoxicity was noticed with dementia in 30% of progression-free patients.

[Article](#) [CAS](#) [PubMed](#) [PubMed Central](#) [Google Scholar](#)

25. Di Perri D, Jmil S, Lawson TM, Van Calster L, Whenham N, Renard L. Health-related quality of life and cognitive failures in patients with lower-grade gliomas treated with radiotherapy. *Cancer Radiother.* 2023;27:219–24. <https://doi.org/10.1016/j.canrad.2022.10.004>.

[Article](#) [PubMed](#) [Google Scholar](#)

26. Desmurget M, Bonnetblanc F, Duffau H. Contrasting acute and slow-growing lesions: a new door to brain plasticity. *Brain.* 2007;130:898–914. <https://doi.org/10.1093/brain/awl300>.

[Article](#) [PubMed](#) [Google Scholar](#)

27. Ng S, Duffau H, Herbet G. Perspectives in human brain plasticity sparked by glioma invasion: from intraoperative (re)mappings to neural reconfigurations. *Neural Regen Res.* 2024;19:947–48. <https://doi.org/10.4103/1673-5374.382246>.

[Article](#) [PubMed](#) [Google Scholar](#)

28. Ng S, Moritz-Gasser S, Lemaitre AL, Duffau H, Herbet G. Multivariate mapping of low-resilient neurocognitive systems within and around low-grade gliomas. *Brain.* 2024 Apr 24:awae130. doi: 10.1093/brain/awae130. Online ahead of print. This series shed new light on both low-resilient neural systems and the prediction of cognitive recovery following glioma surgery, especially after supratotal resection.

29. Duffau H. White matter tracts and diffuse Lower-Grade gliomas: the pivotal role of myelin plasticity in the Tumor Pathogenesis, infiltration patterns, functional consequences and Therapeutic Management. *Front Oncol.* 2022;12(855587). <https://doi.org/10.3389/fonc.2022.855587>. eCollection 2022.

30. Fahlström M, Mirza S, Alberius Munkhammar Å, Zetterling M, Latini F. Qualitative and visual along-tract analysis of diffusion-based parameters in patients with diffuse gliomas. *Brain Sci.* 2024;14:213. <https://doi.org/10.3390/brainsci14030213>.
- [Article](#) [PubMed](#) [PubMed Central](#) [Google Scholar](#)
31. Darlix A, Deverdun J, Menjot de Champfleury N, Castan F, Zouaoui S, Rigau V, et al. IDH mutation and 1p19q codeletion distinguish two radiological patterns of diffuse low-grade gliomas. *J Neurooncol.* 2017;133:37–45. <https://doi.org/10.1007/s11060-017-2421-0>.
- [Article](#) [CAS](#) [PubMed](#) [Google Scholar](#)
32. Alfonso JCL, Talkenberger K, Seifert M, Klink B, Hawkins-Daarud A, Swanson KR, et al. The biology and mathematical modelling of glioma invasion: a review. *J R Soc Interface.* 2017;14:20170490. <https://doi.org/10.1098/rsif.2017.0490>.
- [Article](#) [CAS](#) [PubMed](#) [PubMed Central](#) [Google Scholar](#)
33. Gomez H. Quantitative analysis of the proliferative-to-invasive transition of hypoxic glioma cells. *Integr Biol (Camb).* 2017;9:257–62. <https://doi.org/10.1039/c6ib00208k>.
- [Article](#) [CAS](#) [PubMed](#) [Google Scholar](#)
34. Budia I, Alvarez-Arenas A, Woolley TE, Calvo GF, Belmonte-Beitia J. Radiation protraction schedules for low-grade gliomas: a comparison between different mathematical models. *J R Soc Interface.* 2019;16:20190665. <https://doi.org/10.1098/rsif.2019.0665>.
- [Article](#) [CAS](#) [PubMed](#) [PubMed Central](#) [Google Scholar](#)
35. Ayala-Hernández LE, Gallegos A, Schucht P, Murek M, Pérez-Romasanta L, Belmonte-Beitia J, et al. Optimal combinations of Chemotherapy and Radiotherapy in Low-Grade gliomas: a Mathematical Approach. *J Pers Med.* 2021;11:1036.
- [Article](#) [PubMed](#) [PubMed Central](#) [Google Scholar](#)
36. Hu LS, Hawkins-Daarud A, Wang L, Li J, Swanson KR. Imaging of intratumoral heterogeneity in high-grade glioma. *Cancer Lett.* 2020;477:97–106. <https://doi.org/10.1016/>

[j.canlet.2020.02.025.](#)

[Article](#) [CAS](#) [PubMed](#) [PubMed Central](#) [Google Scholar](#)

37. Zinsz A, Pouget C, Rech F, Taillandier L, Blonski M, Amlal S, et al. The role of [18 F]FDOPA PET as an adjunct to conventional MRI in the diagnosis of aggressive glial lesions. *Eur J Nucl Med Mol Imaging*. 2024;51:2672–83.

[Article](#) [CAS](#) [PubMed](#) [Google Scholar](#)

38. Booth TC, Williams M, Luis A, Cardoso J, Ashkan K, Shuaib H. Machine learning and glioma imaging biomarkers. *Clin Radiol*. 2020;75:20–32. <https://doi.org/10.1016/j.crad.2019.07.001>.

[Article](#) [CAS](#) [PubMed](#) [Google Scholar](#)

39. Fan H, Luo Y, Gu F, Tian B, Xiong Y, Wu G, et al. Artificial intelligence-based MRI radiomics and radiogenomics in glioma. *Cancer Imaging*. 2024;24:36. <https://doi.org/10.1186/s40644-024-00682-y>.

[Article](#) [PubMed](#) [PubMed Central](#) [Google Scholar](#)

40. Gerin C, Pallud J, Deroulers C, Varlet P, Oppenheim C, Roux FX, et al. Quantitative characterization of the imaging limits of diffuse low-grade oligodendrogliomas. *Neuro Oncol*. 2013;15:1379–88. <https://doi.org/10.1093/neuonc/not072>.

[Article](#) [PubMed](#) [PubMed Central](#) [Google Scholar](#)

41. Pedetour-Braccini Z, Burel-Vandenbos F, Gozé C, Roger C, Bazin A, Costes-Martineau V, et al. Microfoci of malignant progression in diffuse low-grade gliomas: towards the creation of an intermediate grade in glioma classification? *Virchows Arch*. 2015;466:433–44. <https://doi.org/10.1007/s00428-014-1712-5>.

[Article](#) [CAS](#) [PubMed](#) [Google Scholar](#)

42. Ghinda DC, Yang Y, Wu S, Lu J, Su L, Damiani S, et al. Personalized Multimodal demarcation of Peritumoral tissue in Glioma. *JCO Precis Oncol.* 2020;4:1128–40. <https://doi.org/10.1200/PO.20.00115>.

[Article](#) [PubMed](#) [Google Scholar](#)

43. Mazor T, Chesnelong C, Pankov A, Jalbert LE, Hong C, Hayes J, et al. Clonal expansion and epigenetic reprogramming following deletion or amplification of mutant IDH1. *Proc Natl Acad Sci USA.* 2017;114:10743–48. <https://doi.org/10.1073/pnas.1708914114>.

[Article](#) [CAS](#) [PubMed](#) [PubMed Central](#) [Google Scholar](#)

44. Bao Z, Wang Y, Wang Q, Fang S, Shan X, Wang J, et al. Intratumor heterogeneity, microenvironment, and mechanisms of drug resistance in glioma recurrence and evolution. *Front Med.* 2021;15:551–61. <https://doi.org/10.1007/s11684-020-0760-2>.

[Article](#) [PubMed](#) [Google Scholar](#)

45. Wang L, Wang H, D'Angelo F, Curtin L, Sereduk CP, De Leon G, et al. Quantifying intra-tumoral genetic heterogeneity of glioblastoma toward precision medicine using MRI and a data-inclusive machine learning algorithm. *PLoS ONE.* 2024;19:e0299267. <https://doi.org/10.1371/journal.pone.0299267>.

[Article](#) [CAS](#) [PubMed](#) [PubMed Central](#) [Google Scholar](#)

46. Dhruv HD, McDonough Winslow WS, Armstrong B, Tuncali S, Eschbacher J et al. Reciprocal activation of transcription factors underlies the dichotomy between proliferation and invasion of glioma cells. *PLoS One.* 2013;8(8):e72134. <https://doi.org/10.1371/journal.pone.0072134>. eCollection 2013.

47. Osswald M, Jung E, Sahm F, Solecki G, Venkataramani V, Blaes J, et al. Brain tumour cells interconnect to a functional and resistant network. *Nature.* 2015;528:93–8. <https://doi.org/10.1038/nature16071>.

[Article](#) [CAS](#) [PubMed](#) [Google Scholar](#)

48. Venkataramani V, Yang Y, Schubert MC, Reyhan E, Tetzlaff SK, Wissmann N et al. Glioblastoma hijacks neuronal mechanisms for brain invasion. *Cell.* 2022;185:2899–2917

e2831. <https://doi.org/10.1016/j.cell.2022.06.054>. By superimposing molecular and functional single-cell data, the authors evidenced that neuronal mechanisms govern glioblastoma cell invasion on multiple levels.

49. Venkataramani V, Schneider M, Giordano FA, Kuner T, Wick W, Herrlinger U, et al. Disconnecting multicellular networks in brain tumours. *Nat Rev Cancer*. 2022;22:481–91. <https://doi.org/10.1038/s41568-022-00475-0>.

[Article](#) [CAS](#) [PubMed](#) [Google Scholar](#)

50. Schneider M, Potthoff AL, Karpel-Massler G, Schuss P, Siegelin MD, Debatin KM et al. The Alcatraz-Strategy: a roadmap to break the connectivity barrier in malignant brain tumours. *Mol Oncol* 2024 Apr 3. <https://doi.org/10.1002/1878-0261.13642>. Online ahead of print.

51. Duffau H. The error of Broca: from the traditional localizationist concept to a connectomal anatomy of human brain. *J Chem Neuroanat*. 2018;89:73–81. <https://doi.org/10.1016/j.jchemneu.2017.04.003>.

[Article](#) [PubMed](#) [Google Scholar](#)

52. Duffau H. A two-level model of interindividual anatomo-functional variability of the brain and its implications for neurosurgery. *Cortex*. 2017;86:303–13. <https://doi.org/10.1016/j.cortex.2015.12.009>.

[Article](#) [PubMed](#) [Google Scholar](#)

53. Herbet G, Duffau H, Mandonnet E. Predictors of cognition after glioma surgery: connectotomy, structure-function phenotype, plasticity. *Brain*. 2024 Apr 4:awae093. <https://doi.org/10.1093/brain/awae093>. Online ahead of print. The authors introduced the concept of connectotomy, which models the glioma resection in the connectivity space, by computing a handful number of networks disconnection indices, measuring how the structural connectivity sustaining each network of interest was hit by the resection.

54. Kong XZ, Mathias SR, Guadalupe T, ENIGMA Laterality Working Group, Glahn DC, Franke B, et al. Mapping cortical brain asymmetry in 17,141 healthy individuals worldwide via the ENIGMA Consortium. PNAS. 2018;115:E5154–63. <https://doi.org/10.1073/pnas.1718418115>.

[Article](#) [CAS](#) [PubMed](#) [PubMed Central](#) [Google Scholar](#)

55. Grasby K, Jahanshad N, Painter JN, Colodro-Conde L, Bralten J, Hibar DP, et al. The genetic architecture of the human cerebral cortex. Science. 2020;367(6484):eaay6690. <https://doi.org/10.1126/science.aay6690>.

[Article](#) [CAS](#) [PubMed](#) [PubMed Central](#) [Google Scholar](#)

56. Eichert N, Watkins KE, Mars RB, Petrides M. Morphological and functional variability in central and subcentral motor cortex of the human brain. Brain Struct Funct. 2021;226:263–79. <https://doi.org/10.1007/s00429-020-02180-w>.

[Article](#) [PubMed](#) [Google Scholar](#)

57. Forkel SJ, Friedrich P, Thiebaut de Schotten M, Howells H. White matter variability, cognition, and disorders: a systematic review. Brain Struct Funct. 2022;227:529–44.

[Article](#) [PubMed](#) [Google Scholar](#)

58. Lebel C, Treit S, Beaulieu C. A review of diffusion MRI of typical white matter development from early childhood to young adulthood. NMR Biomed. 2019;32:e3778. <https://doi.org/10.1002/nbm.3778>.

[Article](#) [PubMed](#) [Google Scholar](#)

59. Hong TY, Yang CJ, Cheng LK, Li WC, Tseng WI, Yeh TC, et al. Enhanced white matter fiber tract of the cortical visual system in visual artists: implications for creativity. Front Neurosci. 2023;17:1248266. <https://doi.org/10.3389/fnins.2023.1248266>.

[Article](#) [PubMed](#) [PubMed Central](#) [Google Scholar](#)

60. Dhakal K, Norgaard M, Dhamala M. Enhanced White Matter Fiber tracts in Advanced Jazz improvisers. *Brain Sci.* 2021;11:506. <https://doi.org/10.3390/brainsci11040506>.

[Article](#) [PubMed](#) [PubMed Central](#) [Google Scholar](#)

61. Cheng LK, Chiu YH, Lin YC, Li WC, Hong TY, Yang CJ, et al. Long-term musical training induces white matter plasticity in emotion and language networks. *Hum Brain Mapp.* 2023;44:5–17. <https://doi.org/10.1002/hbm.26054>.

[Article](#) [PubMed](#) [Google Scholar](#)

62. Munsell BC, Gleichgerrcht E, Hofesmann E, Delgaizo J, McDonald CR, Marebwa B, et al. Personalised connectome fingerprints: their importance in cognition from childhood to adult years. *NeuroImage.* 2020;221:117122. <https://doi.org/10.1016/j.neuroimage.2020.117122>.

[Article](#) [CAS](#) [PubMed](#) [Google Scholar](#)

63. Taebi A, Kiesow H, Vogeley K, Schilbach L, Bernhardt BC, Bzdok D. Population variability in social brain morphology for social support, household size and friendship satisfaction. *Soc Cogn Affect Neurosci.* 2020;15:635–47. <https://doi.org/10.1093/scan/nsaa075>.

[Article](#) [Google Scholar](#)

64. Genon S, Eickhoff SB, Kharabian S. Linking interindividual variability in brain structure to behaviour. *Nat Rev Neurosci.* 2022;23:307–18. <https://doi.org/10.1038/s41583-022-00584-7>.
New perspectives are exposed about the multivariate nature regarding the representation of the relationships between brain structure and behavioural data by latent dimensions of interindividual variability.

[Article](#) [CAS](#) [PubMed](#) [Google Scholar](#)

65. Herbet G, Duffau H. Revisiting the functional anatomy of the human brain: toward a Meta-networking theory of cerebral functions. *Physiol Rev.* 2020;100:1181–228. <https://doi.org/10.1152/physrev.00033.2019>. This comprehensive review introduces the original concept of metanetworking organization underpinning brain functions, based on transient changes of relationship within and across neural networks, able to result in more long-lasting modifications of network properties, including use-dependent neuroplasticity.

[Article](#) [PubMed](#) [Google Scholar](#)

66. Forkel SJ, Rogalski E, Drossinos Sancho N, D'Anna L, Luque Laguna P, Sridhar J, Dell'Acqua F, et al. Anatomical evidence of an indirect pathway for word repetition. *Neurology.* 2020;94:e594–606. <https://doi.org/10.1212/WNL.00000000000008746>.

[Article](#) [PubMed](#) [PubMed Central](#) [Google Scholar](#)

67. Johnson KA, Duffley G, Anderson DN, Ostrem JL, Welter ML, Baldermann JC, et al. Structural connectivity predicts clinical outcomes of deep brain stimulation for Tourette syndrome. *Brain.* 2020;143(8):2607–23. <https://doi.org/10.1093/brain/awaa188>.

[Article](#) [PubMed](#) [PubMed Central](#) [Google Scholar](#)

68. Lunven M, Rode G, Bourlon C, Duret C, Migliaccio R, Chevrillon E, et al. Anatomical predictors of successful prism adaptation in chronic visual neglect. *Cortex.* 2019;120:629–41. <https://doi.org/10.1016/j.cortex.2018.12.004>.

[Article](#) [PubMed](#) [Google Scholar](#)

69. Parlatini V, Radua J, Solanes Font A, Wichers R, Maltezos S, Sanefuji M, et al. Poor response to methylphenidate is associated with a smaller dorsal attentive network in adult Attention-Deficit/Hyperactivity disorder (ADHD). *Transl Psychiatry.* 202;13(303). <https://doi.org/10.1038/s41398-023-02598-w>.

70. Cargnelutti E, Ius T, Skrap M, Tomasino B. Plasticity review what do we know about pre- and postoperative plasticity in patients with glioma? A review of neuroimaging and intraoperative mapping studies. *Neuroimage Clin.* 2020;28:102435. <https://doi.org/10.1016/j.nicl.2020.102435>.

[Article](#) [PubMed](#) [PubMed Central](#) [Google Scholar](#)

71. Hart M, Romero-Garcia R, Price SJ, Suckling J. Global effects of focal brain tumors on functional complexity and network robustness: a prospective cohort study. *Neurosurgery*. 2019;84:1201–13. <https://doi.org/10.1093/neuros/nyy378>.

[Article](#) [PubMed](#) [Google Scholar](#)

72. Duffau H. Functional mapping before and after low-Grade glioma surgery: a New Way to decipher various spatiotemporal patterns of individual neuroplastic potential in Brain Tumor patients. *Cancers (Basel)*. 2020;12:2611. <https://doi.org/10.3390/cancers12092611>.

[Article](#) [CAS](#) [PubMed](#) [Google Scholar](#)

73. Almairac F, Duffau H, Herbet G. Contralesional macrostructural plasticity of the insular cortex in patients with glioma: a VBM study. *Neurology*. 2018;91:e1902–8. <https://doi.org/10.1212/WNL.0000000000006517>.

[Article](#) [PubMed](#) [Google Scholar](#)

74. Almairac F, Deverdun J, Cochereau J, Coget A, Lemaitre AL, Moritz-Gasser S, et al. Homotopic redistribution of functional connectivity in insula-centered diffuse low-grade glioma. *Neuroimage Clin*. 2021;29:102571. <https://doi.org/10.1016/j.nicl.2021.102571>.

[Article](#) [PubMed](#) [PubMed Central](#) [Google Scholar](#)

75. Liu D, Chen J, Ge H, Yan Z, Luo B, Hu X, et al. Structural plasticity of the contralesional hippocampus and its subfields in patients with glioma. *Eur Radiol*. 2023;33:6107–15. <https://doi.org/10.1007/s00330-023-09582-4>.

[Article](#) [PubMed](#) [Google Scholar](#)

76. Lv K, Cao X, Wang R, Lu Q, Wang J, Zhang J, et al. Contralesional macrostructural plasticity in patients with frontal low-grade glioma: a voxel-based morphometry study. *Neuroradiology*. 2023;65:297–305. <https://doi.org/10.1007/s00234-022-03059-9>.

[Article](#) [PubMed](#) [Google Scholar](#)

77. Pasquini L, Yildirim O, Silveira P, Tamer C, Napolitano A, Lucignani M, et al. Effect of tumor genetics, pathology, and location on fMRI of language reorganization in brain tumor patients. *Eur Radiol*. 2023;33(9):6069–78. <https://doi.org/10.1007/s00330-023-09610-3>.

[Article](#) [CAS](#) [PubMed](#) [PubMed Central](#) [Google Scholar](#)

78. Ng S, Deverdun J, Lemaitre AL, Giampiccolo D, Bars EL, Moritz-Gasser S, et al. Precuneal gliomas promote behaviorally relevant remodeling of the functional connectome. *J Neurosurg.* 2022;138:1531–41. <https://doi.org/10.3171/2022.9.JNS221723>.

[Article](#) [PubMed](#) [Google Scholar](#)

79. Duffau H. Nuancing the Limitations of Axonal Plasticity in World Health Organization Grade II gliomas: White Matter tracts compensation is driven by cortical remodeling. *Neurosurgery.* 2023;93:e85–91. <https://doi.org/10.1227/neu.0000000000002508>.

[Article](#) [PubMed](#) [Google Scholar](#)

80. Ius T, Angelini E, Thiebaut de Schotten M, Mandonnet E, Duffau H. Evidence for potentials and limitations of brain plasticity using an atlas of functional resectability of WHO grade II gliomas: towards a minimal common brain. *NeuroImage.* 2011;56:992–1000. <https://doi.org/10.1016/j.neuroimage.2011.03.022>.

[Article](#) [PubMed](#) [Google Scholar](#)

81. Herbet G, Maheu M, Costi E, Lafargue G, Duffau H. Mapping neuroplastic potential in brain-damaged patients. *Brain.* 2016;139:829–44. <https://doi.org/10.1093/brain/awv394>.

[Article](#) [PubMed](#) [Google Scholar](#)

82. Duffau H. Damaging a few millimeters of the deep white matter tracts during glioma surgery may result in a large-scale brain disconnection. *J Neurosurg.* 2023;140:311–14. <https://doi.org/10.3171/2023.6.JNS231048>.

[Article](#) [PubMed](#) [Google Scholar](#)

83. Zotey V, Andhale A, Shegekar T, Juganavar A. Adaptive neuroplasticity in Brain Injury Recovery: strategies and insights. *Cureus.* 2023;15:e45873. <https://doi.org/10.7759/cureus.45873>.

[Article](#) [PubMed](#) [PubMed Central](#) [Google Scholar](#)

84. Renner J, Rasia-Filho AA. Morphological features of human dendritic spines. *Adv Neurobiol.* 2023;34:367–496. https://doi.org/10.1007/978-3-031-36159-3_9.
[Article](#) [PubMed](#) [Google Scholar](#)
85. Uyeda A, Muramatsu R. Molecular mechanisms of Central Nervous System Axonal Regeneration and Remyelination: a review. *Int J Mol Sci.* 2020;21:8116. <https://doi.org/10.3390/ijms21218116>.
[Article](#) [CAS](#) [PubMed](#) [PubMed Central](#) [Google Scholar](#)
86. Stampanoni Bassi M, Iezzi E, Gilio L, Centonze D, Buttari F. Synaptic plasticity shapes Brain Connectivity: implications for Network Topology. *Int J Mol Sci.* 2019;20:6193. <https://doi.org/10.3390/ijms20246193>.
[Article](#) [CAS](#) [PubMed](#) [PubMed Central](#) [Google Scholar](#)
87. Makin TR, Krakauer JW. Against cortical reorganisation. *eLife.* 2023;12:e84716. <https://doi.org/10.7554/eLife.84716>.
[Article](#) [CAS](#) [PubMed](#) [PubMed Central](#) [Google Scholar](#)
88. Venkatesh HS, Morishita W, Geraghty AC, Silverbush D, Gillespie SM, Arzt M, et al. Electrical and synaptic integration of glioma into neural circuits. *Nature.* 2019;573:539–45. <https://doi.org/10.1038/s41586-019-1563-y>.
[Article](#) [CAS](#) [PubMed](#) [PubMed Central](#) [Google Scholar](#)
89. Mancusi R, Monje M. The neuroscience of cancer. *Nature.* 2023;618:467–79. <https://doi.org/10.1038/s41586-023-05968-y>. In gliomas, through neuron-to-cancer cell synapses, the nervous system can regulate cancer progression, while cancer also remodels and hijacks nervous system structure and function.
[Article](#) [CAS](#) [PubMed](#) [PubMed Central](#) [Google Scholar](#)
90. Just N, Chevillard PM, Migaud M. Imaging and spectroscopic methods to investigate adult neurogenesis in vivo: New models and new avenues. *Front Neurosci.* 2022;16:933947. <https://doi.org/10.3389/fnins.2022.933947>.

[Article](#) [PubMed](#) [PubMed Central](#) [Google Scholar](#)

91. Novikov DS. The present and the future of microstructure MRI: from a paradigm shift to normal science. *J Neurosci Methods*. 2021;351:108947. <https://doi.org/10.1016/j.jneumeth.2020.108947>.

[Article](#) [PubMed](#) [Google Scholar](#)

92. Sierra A, Gröhn O, Pitkänen A. Imaging microstructural damage and plasticity in the hippocampus during epileptogenesis. *Neuroscience*. 2015;309:162–72. <https://doi.org/10.1016/j.neuroscience.2015.04.054>.

[Article](#) [CAS](#) [PubMed](#) [Google Scholar](#)

93. Becker G, Dammicco S, Bahri MA, Salmon E. The rise of synaptic density PET imaging. *Molecules*. 2020;25:2303. <https://doi.org/10.3390/molecules25102303>.

[Article](#) [CAS](#) [PubMed](#) [PubMed Central](#) [Google Scholar](#)

94. Darlix A, Monnier M, Castan F, Coutant L, Fabbro M, Denis-Chammas È, et al. Longitudinal assessment of quality of life, neurocognition, and psychopathology in patients with low-grade glioma on first-line temozolomide: a feasibility study. *Neurooncol Adv*. 2024;6:vdae084. <https://doi.org/10.1093/noajnl/vdae084>.

[Article](#) [PubMed](#) [PubMed Central](#) [Google Scholar](#)

95. Mellinghoff IK, van den Bent MJ, Blumenthal DT, Touat M, Peters KB, Clarke J, et al. Vorasidenib in IDH1- or IDH2-Mutant low-Grade Glioma. *N Engl J Med*. 2023;389:589–601. <https://doi.org/10.1056/NEJMoa2304194>.

[Article](#) [CAS](#) [PubMed](#) [PubMed Central](#) [Google Scholar](#)

96. Ribeiro L, Ng S, Duffau H. Recurrent insular low-grade gliomas: factors guiding the decision to reoperate. *J Neurosurg*. 2022;138:1216–26. <https://doi.org/10.3171/2022.9.JNS221286>.

[Article](#) [PubMed](#) [Google Scholar](#)

97. Ferracci FX, Michaud K, Duffau H. The landscape of postsurgical recurrence patterns in diffuse

low-grade gliomas. *Crit Rev Oncol Hematol*. 2019;138:148–55. <https://doi.org/10.1016/j.critrevonc.2019.04.009>.

[Article](#) [PubMed](#) [Google Scholar](#)

98. Ng S, Valdes PA, Moritz-Gasser S, Lemaitre AL, Duffau H, Herbet G. Intraoperative functional remapping unveils evolving patterns of cortical plasticity. *Brain*. 2023;146:3088–100. <https://doi.org/10.1093/brain/awad116>. These original results provide a critical insight into the dynamic potential of low grade glioma-induced continuing rearrangements of the cerebral cortex, with considerable implications for re-operations.
99. Hamdan N, Duffau H. Extending the multistage surgical strategy for recurrent initially low-grade gliomas: functional and oncological outcomes in 31 consecutive patients who underwent a third resection under awake mapping. *J Neurosurg*. 2022;136:1035–44. <https://doi.org/10.3171/2021.3.JNS21264>.

[Article](#) [PubMed](#) [Google Scholar](#)

100. Lemaitre AL, Herbet G, Ng S, Moritz-Gasser S, Duffau H. Cognitive preservation following awake mapping-based neurosurgery for low-grade gliomas: A longitudinal, within-patient design study. *Neuro-Oncol*. 2022;24:781–93. <https://doi.org/10.1093/neuonc/noab275>. Systematic longitudinal neuropsychological assessments performed before and after awake surgery for low-grade glioma evidenced that 86% of patients had no cognitive decline despite large resections and that only 5.8% did not return to work.
101. Darlix A, Gozé C, Rigau V, Bauchet L, Taillandier L, Duffau H. The etiopathogenesis of diffuse low-grade gliomas. *Crit Rev Oncol Hematol*. 2017;109:51–62. <https://doi.org/10.1016/j.critrevonc.2016.11.014>.

[Article](#) [PubMed](#) [Google Scholar](#)

102. Duffau H. A personalized longitudinal strategy in low-Grade Glioma patients: Predicting Oncological and neural interindividual variability and its changes over years to think one step ahead. *J Pers Med*. 2022;12:1621. <https://doi.org/10.3390/jpm12101621>.

[Article](#) [PubMed](#) [PubMed Central](#) [Google Scholar](#)

103. Ius T, Ng S, Young JS, Tomasino B, Polano M, Ben-Israel D, Kelly JJP, Skrap M, Duffau H,

Berger MS. The benefit of early surgery on overall survival in incidental low-grade glioma patients: a multicenter study. *Neuro Oncol.* 2022;24:624–38. <https://doi.org/10.1093/neuonc/noab210>.

[Article](#) [PubMed](#) [Google Scholar](#)

104. Duffau H. Dynamic interplay between Lower-Grade Glioma instability and brain metaplasticity: proposal of an original model to Guide the Therapeutic Strategy. *Cancers (Basel).* 2021;13:4759. <https://doi.org/10.3390/cancers13194759>.

[Article](#) [PubMed](#) [Google Scholar](#)

105. Boccuni L, Abellaneda-Pérez K, Martín-Fernández J, Leno-Colorado D, Roca-Ventura A, Prats Bisbe A, et al. Neuromodulation-induced prehabilitation to leverage neuroplasticity before brain tumor surgery: a single-cohort feasibility trial protocol. *Front Neurol.* 2023;14:1243857. <https://doi.org/10.3389/fneur.2023.1243857>.

[Article](#) [PubMed](#) [PubMed Central](#) [Google Scholar](#)

Author information

Authors and Affiliations

Department of Neurosurgery, Gui de Chauliac Hospital, Montpellier University Medical Center, 80 Avenue Augustin Fliche, Montpellier, 34295, France

Hugues Duffau

Team “Plasticity of Central Nervous System, Stem Cells and Low-grade Gliomas,” INSERM U1191, Institute of Functional Genomics, University of Montpellier, Montpellier, France

Hugues Duffau

Contributions

H.D. wrote the main manuscript, prepared Figs. 1 and 2 and reviewed the manuscript.

Corresponding author

Correspondence to [Hugues Duffau](#).

Ethics declarations

Competing Interests

The authors declare no competing interests.

Human and Animal Rights and Informed Consent

This article does not contain any studies with human or animal subjects performed by the author.

Additional information

Publisher's Note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

The future is a door, the past is the key (Victor Hugo).

Rights and permissions

Springer Nature or its licensor (e.g. a society or other partner) holds exclusive rights to this article under a publishing agreement with the author(s) or other rightsholder(s); author self-archiving of the accepted manuscript version of this article is solely governed by the terms of such publishing agreement and applicable law.

[Reprints and permissions](#)

About this article

Cite this article

Duffau, H. Neuroplasticity in Diffuse Low-grade Gliomas: Backward Modelling of Brain-tumor Interactions Prior to Diagnosis is Needed to Better Predict Recovery after Treatment. *Curr Neurol Neurosci Rep* 25, 15 (2025). <https://doi.org/10.1007/s11910-024-01402-6>

Accepted

30 December 2024

Published

09 January 2025

DOI

<https://doi.org/10.1007/s11910-024-01402-6>

Keywords

[Brain-tumor interplay](#)

[Connectome](#)

[Diffuse glioma](#)

[Low-grade glioma](#)

[Neuroplasticity](#)

[Personalized management](#)

[Surgery](#)