Editors’ Note: Is synthetic cannabis more likely than pure cannabis to be associated with stroke? McSherry raises an interesting question. Chamberlain points out that the glioma biomarker ATRX (α-thalassemia/mental retardation syndrome X-linked) gene was not mentioned in the study by Wick et al. on the value of methylguanine methyltransferase (MGMT) in gliomas. The authors respond and discuss the role of ATRX and its interaction with MGMT and IDH1 (isocitrate dehydrogenase 1).

—Chafic Karam, MD, and Robert C. Griggs, MD

SPICE, POT, AND STROKE
Joseph W. McSherry, Burlington, VT: In the last paragraph of his editorial, Dr. Brust1 seemed doubtful of anecdotal reports of stroke in marijuana users, given common cannabis usage and lack of reports. Freeman et al.2 reported 2 persons using spice with associated vascular events. In the future, it will be important to clarify when a stroke in a cannabis user may be due to use of synthetic CB1 agonists. The paucity of cannabis stroke articles in the 1960s and 1970s contrasts to recent articles showing enhanced stroke risk in “cannabis” users. Those using both the natural plant and synthetic forms may be at risk as the synthetic form is not detected on typical drug screens. The unavailability of pure cannabis may lead to increased strokes and a public health problem.


PROGNOSTIC OR PREDICTIVE VALUE OF MGMT PROMOTER METHYLATION IN GLIOMAS DEPENDS ON IDH1 MUTATION
Marc C. Chamberlain, Seattle: Wick et al.1 determined that the interaction of molecular markers (methylguanine methyltransferase [MGMT], isocitrate dehydrogenase 1 [IDH1], and loss of chromosomes 1p and 19q) in anaplastic gliomas (AG) was a hypothesis-generating analysis. This is because examination of interactive biomarkers was never prespecified as an endpoint in the NOA-04 trial.2 Biomarker determination segregates AG into 2 categories based on presence or absence of 1p19q co-deletion.3 MGMT methylation or IDH1 mutation does not modify the prognostic and predictive value of 1p19q co-deletion. The suggested interaction is novel between IDH1 and MGMT in the larger cohort of AG that is not codeleted. In IDH1 wild-type AG, patients with MGMT promoter methylation derive greater benefit from temozolomide, whereas patients without MGMT methylation derive greater benefit from radiotherapy.4

The authors did not mention the glioma biomarker ATRX (α-thalassemia/mental retardation syndrome X-linked) gene, which regulates chromatin remodeling. It is mutated in gliomas of astrocytic lineage, is mutually exclusive with 1p19q codeletion, and may be both prognostic and predictive.5 Determining the interaction of ATRX with IDH1 and MGMT will provide further insight into the utility of these glioma biomarkers.

Author Response: Wolfgang Wick, Michael Platten, Heidelberg; Guido Reifenberger, Düsseldorf, Germany; Michael Weller, Zurich: In the NOA-04 biomarker cohort, loss of ATRX expression is seen in anaplastic astrocytomas (45%) (AA), oligoastrocytomas (AOA) (27%), and oligodendrogliomas (AO) (10%). It is mainly restricted to IDH mutant tumors and almost mutually exclusive to the 1p/19q codeletion.6 It is inversely correlated with hotspot mutations in the promoter region of telomerase reverse transcriptase (TERT).7 ATRX may be suitable to regroup AOA into 2 distinct entities with favorable prognosis. Clinically, AOA with ATRX loss are similar to AA with good prognosis, whereas AOA carrying 1p/19q codeletion are indistinguishable from AO. AA with the IDH mutation are further stratified by ATRX, with the loss providing a better prognosis.6 While fitting these data into the interaction term used for the MGMT/IDH analysis1 is formally restricted due to the high number of necessary events for this triple interaction, we see a need for IDH testing in AG. For clinical decision-making, we assess O6-MGMT status
Spice, pot, and stroke
Joseph W. McSherry
Neurology 2014;82;2147
DOI 10.1212/WNL.0000000000000508

This information is current as of June 9, 2014

Updated Information & Services
including high resolution figures, can be found at:
http://n.neurology.org/content/82/23/2147.1.full

References
This article cites 2 articles, 2 of which you can access for free at:
http://n.neurology.org/content/82/23/2147.1.full#ref-list-1

Permissions & Licensing
Information about reproducing this article in parts (figures, tables) or in its entirety can be found online at:
http://www.neurology.org/about/about_the_journal#permissions

Reprints
Information about ordering reprints can be found online:
http://n.neurology.org/subscribers/advertise