Cannabis and Stroke
Systematic Appraisal of Case Reports

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Background and Purpose—An increasing number of case reports link cannabis consumption to cerebrovascular events. Yet these case reports have not been scrutinized using criteria for causal inference.

Methods—All case reports on cannabis and cerebrovascular events were retrieved. Four causality criteria were addressed: temporality, adequacy of stroke work-up, effects of rechallenge, and concomitant risk factors that could account for the cerebrovascular event.

Results—There were 34 case reports on 64 patients. Most cases (81%) exhibited a temporal relationship between cannabis exposure and the index event. In 70%, the evaluation was sufficiently comprehensive to exclude other sources for stroke. About a quarter (22%) of patients had another stroke after subsequent re-exposure to cannabis. Finally, half of patients (50%) had concomitant stroke risk factors, most commonly tobacco (34%) and alcohol (11%) consumption.

Conclusions—Many case reports support a causal link between cannabis and cerebrovascular events. This accords well with epidemiological and mechanistic research on the cerebrovascular effects of cannabis. **(*Stroke*. 2015;46:852-856. DOI: 10.1161/STROKEAHA.115.008680.)**

Key Words: case management ■ epidemiology ■ risk factors ■ stroke ■ substance-related disorders

Cannabis sativa is the most popular illicit drug consumed in Western societies. This is, in part, because of an assumption among users that cannabis is a safe recreational drug. Conversely, several experts think that cannabis is a risk factor for stroke and its use should be minimized.[1] This perspective is largely premised on case reports linking cannabis exposure to stroke.

One concern is that these case reports have not been formally rated using causality criteria. In particular, the following questions have not been synthesized across the case reports: (1) Was there a temporal relationship between cannabis exposure and the stroke or transient ischemic attack? (2) Were other potential stroke causes excluded through a detailed stroke work-up? (3) Were additional risk factors present that could have explained the stroke (eg, coingested illicit substances)? (4) Was rechallenge with cannabis associated with recurrent stroke? These criteria are based on the Naranjo probability scale for inferring drug-associated causality for adverse events.[2]

Methods

This systematic review adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses. The search combined keywords for cannabis and cerebrovascular disease and was executed in Medline and EMBASE from inception until November 30, 2014 (see Appendix in the online-only Data Supplement for the detailed search strategy). Conference abstracts were permitted. To be included, cases had to undergo parenchymal imaging.

A temporal relationship was defined as a stroke or transient ischemic attack ensuing within 24 hours of consumption of cannabis. A detailed stroke work-up entailed computed tomographic angiography, magnetic resonance angiography, or catheter angiography with parenchymal imaging; blood testing for thrombophilia and vasculitis; and cardiac work-up involving prolonged electrocardiographic monitoring and transthoracic or transesophageal echocardiography. All information for this review was collected from the published case reports themselves.

Results

A total of 989 citations were identified; after relevance screening, the full text of 56 articles were retrieved (Figure). Of these, 34 published case reports or case series were eligible, representing a total of 64 patients (Table; Table I in the online-only Data Supplement).[3–36] Most cases were men (80%); the median age was 32 (range 15–64) years. The majority of infarctions occurred in the anterior circulation (56%); 3 cases involved both anterior and posterior circulations (5%); and the remainder either occurred in the posterior circulation (36%) or were not classified (3%).

Most cases (81%) exhibited a temporal relationship between cannabis exposure and the index cardiovascular event. In 70% of cases, the evaluation was sufficiently comprehensive to exclude other sources of stroke. About a quarter of patients (22%) had recurrent stroke from subsequent re-exposure to

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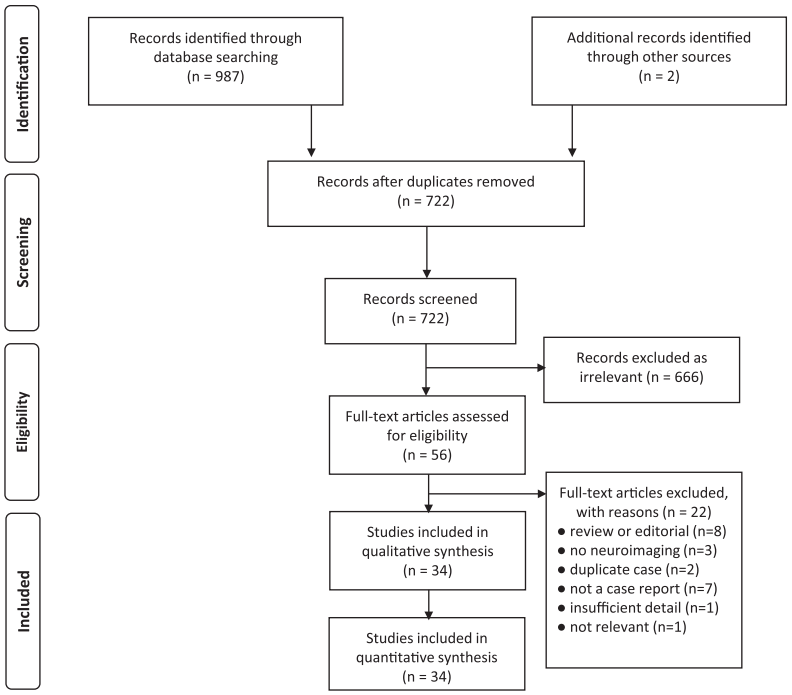

Figure. Literature search and selection.

cannabis. Half of patients (50%) had concomitant risk factors for stroke, most commonly tobacco (34%) and alcohol (11%). Three quarters of patients (48 of 64) underwent toxicological analysis for common street drugs; results were positive for drugs other than cannabis in only 2 cases (Table II in the online-only Data Supplement).

Table. Case Reports With Causality Appraisal

Report	Year Published	Age, y/Sex	Territory of Infarct	Temporality	Other Causes of Stroke Excluded	Concomitant Stroke Risk Factors	Subsequent Re-exposure and Effect
Alvaro et al[3]	2002	33/M	Right PCA	Yes	Yes	Acute coital cephalgia	…
Baharnoori et al[4]	2014	22/M	Right lentiform nucleus and corona radiata	Yes	Yes	None	…
Bal et al[5]	2009	22/M	Bilateral cerebellum and left temporal lobe	Yes	Yes	None	…
Barnes et al[6]	1992	30/M	Left cerebellar hemisphere; left striatocapsular area	Yes	Yes	Tobacco	Stroke
Drumm et al (1)[7]	2012	34/F	Multiple arterial territories	Yes	Yes	Unclear	Stroke
Drumm et al (2)[7]	2012	29/F	Multiple arterial territories	Yes	Yes	Unclear	Stroke
Drumm et al (3)[7]	2012	64/M	Right MCA	Yes	Yes	Unclear	Stroke
El Scheich et al[8]	2013	16/M	Adjacent to the internal capsule at the lateral portion of the left thalamus	Yes	No	Anabolic steroid	…
Finsterer et al[9]	2004	37/M	Right occipital subcortex	Yes	Yes	Tobacco, mild dyslipidemia	…
Giray et al[10]	2011	35/M	Left MCA	No	No	None	…
Haubrich et al[11]	2005	50/M	Left parietal subcortex	Yes	Yes	Hypertension, tobacco	…
Ibrir et al[12]	2014	34/M	Left sylvian fissure	No	Yes	Tobacco, alcohol	…
Inal et al[13]	2014	23/M	Left temporal lobe	No	Yes	Tobacco, alcohol	…
Lawson and Rees[14]	1996	22/M	Right posterior external capsule, upper part of the internal capsule and corona radiata	Yes	No	Tobacco, alcohol, LSD	…
Maguire et al[15]	2011	40/M	Left dorsolateral frontal cortex	No	No	Amphetamine, alcohol, diazepam, tobacco	…

(*Continued*)

Table. Continued

Report	Year Published	Age, y/Sex	Territory of Infarct	Temporality	Other Causes of Stroke Excluded	Concomitant Stroke Risk Factors	Subsequent Re-exposure and Effect
Marinella[16]	2001	18/M	Right occipital lobe	Yes	No	Factor V Leiden	…
Mateo et al[17]	2005	36/M	Left temporal and right parietal, left/right frontal, right posterior-temporal and lower parietal	Yes	Yes	Alcohol	Stroke x 2
McCarron and Thomas[18]	1997	29/M	Right MCA	No	No	Tobacco, alcohol	…
Mesec et al[19]	2001	23/M	Left cerebral hemisphere	Yes	No	Tobacco, alcohol	…
Mouzak et al (1)[20]	2000	18/M	Leukoariosis	Yes	Yes	Tobacco	…
Mouzak et al (2)[20]	2000	26/M	Leukoariosis	Yes	Yes	Tobacco	…
Mouzak et al(3)[20]	2000	30/M	Leukoariosis	Yes	Yes	None	…
Nouh et al[21]	2014	32/F	Bilateral occipital infarcts	Yes	Yes	Migraines	…
Oyinloye et al[22]	2014	26/M	Left corpus striatum and insula cortex	Yes	Yes	None	…
Pazderska et al[23]	2009	35/F	Multiple arterial territories (especially right frontal lobe)	No	No	Tobacco, cocaine	Stroke x 2
Reece[24]	2009	56/M	Parieto-occipital cortex	No	No	Mild hypertension, tobacco	…
Renard and Gaillard[25]	2008	34/F	Right temporal lobe hemorrhage	Yes	Yes	Tobacco, buprenorphine	…
Renard et al[26]	2012	33/M	Right MCA and bilateral ACA-MCA watershed zones	No	Yes	Tobacco	…
Russmann et al[27]	2002	27/M	Left MCA	Yes	No	Chemotherapy, tobacco	…
Santos et al[28]	2014	27/M	Left basal ganglia; right lenticulostriate area; right frontal and parietal (ACA and MCA)	No	Yes	None	Stroke x 2
Singh (1)[29]	2012	15/M	Right cerebellum	Yes	Yes	None specified	…
Singh et al (2)[29]	2012	16/M	Bilateral cerebellum	No	Yes	None specified	…
Singh et al (3)[29]	2012	17/M	Left cerebellum	Yes	Yes	None specified	…
Singh et al (4)[29]	2012	22/M	Right cerebellum	Yes	Yes	None specified	Stroke
Singh et al (5)[29]	2012	27/F	Left MCA branch	Yes	Yes	Tobacco	…
Singh et al (6)[29]	2012	28/F	Right cerebellum	Yes	Yes	None specified	…
Singh et al (7)[29]	2012	37/M	Left MCA branch	Yes	Yes	None specified	…
Singh et al (8)[29]	2012	44/M	Bilateral cerebellum	Yes	No	None specified	Stroke
Singh et al (9)[29]	2012	44/F	Left MCA branch	Yes	No	None specified	…
Singh et al (10)[29]	2012	49/M	Right MCA branch	Yes	Yes	None specified	…
Singh et al (11)[29]	2012	52/F	Right MCA/ACA	Yes	No	Hypertension, tobacco	…
Singh et al (12)[29]	2012	50/M	Bilateral cerebellum	Yes	Yes	Hypertension	Stroke
Singh et al (13)[29]	2012	56/M	Right PCA and cerebellum	Yes	No	PFO	Stroke
Singh et al (14)[29]	2012	58/M	Left MCA branch	Yes	No	Tobacco	…
Singh et al (15)[29]	2012	59/M	Pons	Yes	No	Hypertension, previous stroke	…
Singh et al (16)[29]	2012	61/M	Left PCA	Yes	No	Previous stroke	Stroke
Singh et al (17)[29]	2012	63/M	Left MCA branch	Yes	No	Hypertension, previous stroke	…
Smaoui et al[30]	2014	42/M	Left frontal lobe	Yes	No	None specified	…
Terceno et al[31]	2013	37/M	Bilateral MCA and PCA infarctions	No	Yes	Unclear	…
Termote et al[32]	2007	27/M	Left mesencephalon	Unclear	Yes	Alcohol, tobacco	…
Trojak et al[33]	2011	24/M	Insular mantle, lenticular and caudate nuclear structures	Yes	Yes	None	…
Tsivgoulis et al[34]	2014	42/M	Left putamen	Yes	Yes	None	…
Wolff et al (1)[35]	2011	21/M	Vertebrobasilar	Yes	Yes	Unclear	…

(*Continued*)

Table. Continued

Report	Year Published	Age, y/Sex	Territory of Infarct	Temporality	Other Causes of Stroke Excluded	Concomitant Stroke Risk Factors	Subsequent Re-exposure and Effect
Wolff et al (2)[35]	2011	19/M	Vertebrobasilar	Yes	Yes	Unclear	…
Wolff et al (3)[35]	2011	24/F	Vertebrobasilar	Yes	Yes	Unclear	…
Wolff et al (4)[35]	2011	31/F	Anterior circulation	Yes	Yes	Unclear	…
Wolff et al (5)[35]	2011	37/M	Vertebrobasilar	Yes	Yes	Unclear	…
Wolff et al (6)[35]	2011	26/F	Vertebrobasilar	Yes	Yes	Unclear	…
Wolff et al (7)[35]	2011	31/M	Anterior circulation	Yes	Yes	Unclear	…
Wolff et al (8)[35]	2011	44/M	Anterior circulation	Yes	Yes	Unclear	Stroke
Wolff et al (9)[35]	2011	29/M	Vertebrobasilar	Yes	Yes	Unclear	…
Wolff et al (10)[35]	2011	21/F	Vertebrobasilar	Yes	Yes	Unclear	…
Zachariah (1)[36]	1991	34/M	Right basal ganglia and frontoparietal	Yes	Yes	Tobacco	Worsened deficit
Zachariah (2)[36]	1991	32/M	Left basal ganglia and parietal lobe	Yes	Yes	Tobacco	…

ACA indicates anterior cerebral artery; LSD, lysergic acid diethylamide; MCA, middle cerebral artery; and PCA, posterior cerebral artery.

Discussion

This review suggests that the case reports linking cannabis with acute stroke are relatively robust, with high rates of temporality, exclusion of other causes of stroke, and substantial stroke recurrence in patients who resumed cannabis consumption during follow-up. In half, there were concomitant risk factors, such as tobacco and alcohol consumption. However, even if all criteria were met, only a prospective epidemiological study could prove a causal association.

Two epidemiological studies have studied this association. In a large study of hospital admissions in Texas, cannabis exposure was associated with ischemic stroke even after adjusting for alcohol and tobacco (adjusted odds ratio, 1.76; 95% confidence interval, 1.15–2.71).[37] Second, in a prospective case–control study with adjustment for age, sex, and ethnicity, cannabis was associated with the composite of cerebrovascular events (odds ratio, 2.30; 95% confidence interval, 1.08–5.08).[38] Yet after further adjustment for tobacco, the association was weakened (odds ratio, 1.59; 95% confidence interval, 0.71–3.70).

A recent French pharmacovigilance study of cannabis complications detected 3 cerebral complications among a pool of 35 cardiovascular-related cases of cannabis toxicity reported to a central network.[39] The 3 cerebral complications were acute cerebral angiopathy, transient cortical blindness, and spasm of the cerebral artery. Although these 3 cases recovered, there was an overall mortality rate of 25.6% for cardiovascular complications related to cannabis.

Given broad exposure to cannabis in the general population, it is striking that more strokes do not occur among cannabis users. There may be modulation by dose, frequency, strength (% tetrahydrocannabinol), genetic susceptibility, and coingestants. It is possible that exposure is not mentioned by patients with stroke in emergency departments, or that such exposure is overlooked. Overall, however, it seems clear that physiological, clinical, and epidemiological data converge on an increased stroke risk from cannabis exposure. Heightened clinician awareness of this association, particularly in the treatment of young adults, is necessary for preventing recurrent events from future re-exposure to cannabis.

Disclosures

None.

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SUPPLEMENTAL MATERIAL

Supplemental Appendix: Literature search strategy

In Embase 1974 to 2014 November 30, All Ovid MEDLINE(R) 1946 to Present

1. cerebrovascular disorders/ or exp basal ganglia cerebrovascular disease/ or brain ischemia/ or carotid artery diseases/ or exp carotid artery thrombosis/ or cerebral small vessel diseases/ or exp stroke, lacunar/ or intracranial arterial diseases/ or cerebral arterial diseases/ or infarction, anterior cerebral artery/ or infarction, middle cerebral artery/ or infarction, posterior cerebral artery/ or exp intracranial arteriosclerosis/ or "intracranial embolism and thrombosis"/ or exp intracranial embolism/ or intracranial thrombosis/ or intracranial hemorrhages/ or exp cerebral hemorrhage/ or exp intracranial hemorrhage, hypertensive/ or exp subarachnoid hemorrhage/ or exp stroke/ or exp vertebrobasilar insufficiency/

2. (stroke$1 or carotid$ or intracerebral$ or cerebral$ or cerebro$).mp. [mp=ti, ab, sh, hw, tn, ot, dm, mf, dv, kw, nm, kf, px, rx, ui]

3. 1 or 2

4. (hemp or hemps or ganja or marijuana* or marihuana* or bhang or bhangs or cannabis or hashish* or hash or cannabi).mp. or exp cannabis/ [mp=ti, ab, sh, hw, tn, ot, dm, mf, dv, kw, nm, kf, px, rx, ui]

5. 3 and 4

6. limit 5 to english language

7. limit 6 to animals

8. limit 7 to humans

9. 6 not (7 not 8)

10. remove duplicates from 9

Supplementary Table I. Additional details of case reports

Report	Imaging	Exposure details	Prognosis	Additional features
Zachariah (1)[1]	CT scan x 2, SPECT	onset of stroke symptoms while smoking a marijuana cigarette; recently increased his intake of marijuana	some improvement in hemiparesis; discontinued marijuana smoking	left-sided paresis worsened whenever he smoked marijuana
Zachariah (2)[1]	MRI, CT x 2	onset of stroke symptoms half an hour after smoking a marijuana cigarette; recently increased his intake of marijuana	marked improvement in deficits after 3 months of OT/PT	BP returned to normal within one week on a low-sodium diet
Barnes[2]	CT, MRI, cerebral angiography	smoked marijuana immediately before and even after stroke onset	good recovery; pledged to abstain from marijuana	stroke preceded by three cerebrovascular events with left cerebellar infarct on CT
Lawson[3]	CT	used both cannabis and LSD heavily in the week prior to stroke	making reasonable progress with intensive physiotherapy but still has marked residual weakness	three previous transient events, two while smoking marijuana
McCarron[4]	CT, SPECT, MRA	stroke following a weekend of alcohol and marijuana binging	not specified	polysubstance abuse (alcohol and marijuana); pre-stroke transient neurological events
Mouzak (1)[5]	CT, MRI, MRA, DSA	presented 0.5 h after smoking cannabis with TIA symptoms	not specified	CT/MRI showed small-vessel leukoencephalopathy
Mouzak (2)[5]	CT, MRI, MRA, DSA	presented 3 h after smoking a large amount of cannabis with TIA symptoms	not specified	CT/MRI showed small-vessel leukoencephalopathy
Mouzak (3)[5]	CT, MRI, MRA, DSA	TIA symptoms 10 min after smoking cannabis	not specified	CT/MRI showed small-vessel leukoencephalopathy
Marinella[6]	MRA	smoked marijuana the day of stroke onset	not specified	Factor V Leiden heterozygosity
Mesec[7]	MRI	smoked more than 10 marijuana cigarettes the day preceding admission	some improvement in deficits with rehabilitation	MRA showed evidence of vasospasm (LMCA, LACA)
Alvaro[8]	CT, MRI, cerebral	smoked marijuana 30 minutes prior to stroke onset	persistent deficits; discontinued cannabis	stroke occurred during intercourse with sudden onset headache

	angiogram			
Russmann[9]	CT x 2, MRI	incurred stroke 30 minutes after cannabis inhalation	neurological condition rapidly deteriorated and patient died	Cisplatin-based chemotherapy for testicular carcinoma
Finsterer[10]	CT, MRI	stroke occurred within 15 minutes of smoking marijuana; increased frequency in past 6 months	most symptoms abated except for visual blurring on looking to the left	high cholesterol; chronic marijuana exposure
Haubrich[11]	DSA, MRI	recurrent TIA episodes solely evoked while smoking cannabis	no TIA-like episodes following carotid revascularization	patient asymptomatic at 5-month follow-up
Mateo[12]	MRI/MRA	three ischemic strokes immediately after cannabis consumption on each occasion	full recovery and stability with no further drug consumption	MRA showed diminished caliber of the distal portions of the left middle cerebral artery
Termote[13]	CT, MRI	urine toxicology very strongly positive for cannabinoids and negative for cocaine	not specified	wake-up stroke
Renard[14]	MRI/MRA, CTA	smoking 20-25 cannabis cigarettes per day (recent significant increase)	no recurrence at 6 month follow-up	stroke preceded by acute myocardial infarction
Bal[15]	MRI/MRA	presented with stroke 5 h after consuming seven cigarettes of cannabis	modified Rankin score = 2 at 3 months	decreased caliber of PCA and vertebral artery on MRA
Pazderska[16]	MRI/MRA, cerebral angiogram	three strokes with positive urine toxicology for cannabis	no further infarctions for more than 12 months with abstinence from drugs	temporal artery biopsy showed gross hyperplasia and intimal thickening
Reece[17]	CT	daily consumption of marijuana and hashish oil	patient died 6 months prior to publication of this case report (unclear cause)	patient had 63,875 gram-years of cannabis use in addition to hashish
Giray[18]	MRI/MRA	chronic, regular abuse of high-dose hashish with positive serum toxicology	died in ICU 7 days after admission	prior history of stroke and myocardial infarction
Maguire[19]	CT, MRI/MRA	chronic daily cannabis user with positive urine toxicology for cannabis and benzodiazepines	good recovery of speech, advised to stop illicit drug use	acute mutism secondary to dorsolateral frontal cortex infarct
Trojak[20]	CT, MRI	regular cannabis use (up to 5 cigarettes per day) for four years; on the night before admission had	recurrent tonic-clonic seizures; continued to smoke cannabis occasionally	stroke with severe neuropsychiatric sequelae

		smoked more than 10 cannabis cigarettes		
Wolff (1 - 10)[21]	MRI, MRA or CTA ± cerebral angiography	during the days before stroke, all binged on cannabis	six stopped cannabis with a favorable outcome without relapse; in the three who still smoked cannabis, one had a new ischemic stroke, and 2 had a favorable outcome without relapse	all patients had multifocal intracranial stenosis on imaging
Drumm (1)[22]	MRI	cannabis use within 24 hours of stroke	not stated	recurrent stroke with popliteal and renal infarcts
Drumm (2)[22]	MRI	cannabis use within 24 hours of stroke	not stated	recurrent stroke, carotid vasculopathy on ultrasound
Drumm (3)[22]	MRI	cannabis use within 24 hours of stroke	not stated	recurrent stroke with complete MCA occlusion
Renard[23]	CT, MRI	smoked 5 cannabis cigarettes the day of stroke (including one cigarette 50 minutes after headache onset)	by three months later, angiography had normalized	diffuse multifocal arterial narrowing seen on angiography
Singh (1)[24]	CT, autopsy	smoked marijuana the day before admission; urine toxicology positive for THC	died in hospital 22 hours after admission	bilateral acute cerebellar infarcts
Singh (2)[24]	CT, autopsy	smoked marijuana the night before his initial symptoms	died in hospital 12 hours after admission	left cerebellar multivessel infarct
Singh (3)[24]	CT, MRI/MRA, cerebellar biopsy, angiography	smoked marijuana continuously for several days prior to and including the day symptoms developed	at several weeks post-discharge had only mild dysdiadochokinesia	right cerebellar multivessel infarct
Singh (4)[24]	CTA	onset of symptoms during exposure	ataxia with re-exposure to cannabis	right cerebellar infarct
Singh (5)[24]	MRA	onset of symptoms during exposure	discharged home; no stroke on follow-up	left MCA branch infarct
Singh (6)[24]	MRA	onset of symptoms 30 min after exposure	entered rehabilitation; follow-up not available	right cerebellar infarct
Singh (7)[24]	MRA	onset of symptoms during exposure	entered rehabilitation; no recurrence over 1 year of follow-up	left MCA branch infarct
Singh (8)[24]	MRA	onset of symptoms during exposure	ataxia with re-exposure	bilateral cerebellar infarct

Singh (9)[24]	not stated	onset of symptoms 30 min after exposure	entered rehabilitation; follow-up not available	left MCA branch infarct; normal carotid Doppler
Singh (10)[24]	MRA	onset of symptoms during exposure	entered rehabilitation; follow-up not available	right MCA branch infarct; right MCA stenosis on MRA
Singh (11)[24]	MRA	onset of symptoms during exposure	entered rehabilitation; follow-up not available	right MCA/ACA hemodynamic infarct
Singh (12)[24]	MRI/MRA	onset of symptoms during exposure	ataxia with re-exposure	bilateral cerebellar infarcts
Singh (13)[24]	MRA	onset of symptoms during exposure	left hemiparesis with re-exposure	right PCA and cerebellar infarct
Singh (14)[24]	not stated	onset of symptoms during exposure	discharged to home; follow-up not available	left MCA branch infarct
Singh (15)[24]	not stated	onset of symptoms 30 min after exposure	entered rehabilitation; follow-up not available	pontine infarct
Singh (16)[24]	MRA	onset of symptoms during exposure	right hemiparesis with re-exposure	left PCA infarct
Singh (17)[24]	MRA	onset of symptoms during exposure	discharged to skilled nursing; follow-up not available	left MCA branch infarct
El Scheich[25]	CT, MRI/MRA	consumed high dose cannabis on bank holidays and weekends; admitted on a bank holiday	discharged with residual deficits stable over 18 months	additional involvement of anabolic steroid use
Terceno[26]	MRI, TCD	“regular cannabis consumer”	neurological improvement at 3 months; TCD normalized	diagnosis of reversible cerebral vasoconstriction syndrome
Baharnoori[27]	CT/CTA, MRI	onset of symptoms 90 minutes after smoking marijuana	at 2 months, residual deficits but no new events; no longer using cannabis	capsular warning syndrome
Ibrir[28]	MRI/MRA	urine toxicology positive for cannabis	outcome characterized by stabilization	Burger’s disease and ischemic stroke
Inal[29]	CT, MRI	urine toxicology positive for cannabis	follow-up not specified	left temporal lobe infarct
Nouh[30]	MRI, MRA, cerebral angiography	smoked cannabis before the onset of headache	follow-up CT showed improvement of intracranial vasoconstriction	reversible cerebral vasoconstriction syndrome
Oyinloye[31]	CT, MRI/MRA	smoked cannabis three hours prior	lost to follow-up	reduction of the caliber of the left

		to symptom onset		internal carotid artery and occlusion of left middle and anterior cerebral arteries
Santos[32]	CT, MRI/MRA	heavy cannabis user, positive urine toxicology	sustained another infarct with left hemiparesis and positive urine cannabinoids	MRA showed diffuse irregularities of the anterior and posterior circulation
Smaoui[33]	MRI/MRA	used cannabis 6.5 h before onset of symptoms	not stated	reversible cerebral vasoconstriction syndrome
Tsivgoulis[34]	MRI/MRA, TCD	>20-year history of daily cannabis use	free of recurrent events at 8 months off cannabis	MRA showed multifocal intracranial stenosis, which was reversible by 3 months

Supplementary Table II. Details of drug use ascertainment

Report	Synopsis
Zachariah (1)[1]	marijuana smoking by history; denied use of other street drugs and alcohol; analysis of marijuana cigarettes revealed pure cannabis without contaminants
Zachariah (2)[1]	marijuana smoking by history; denies use of alcohol or other street drugs
Barnes[2]	marijuana smoking by history and toxicology (urine testing for cannabis metabolites)
Lawson[3]	marijuana smoking, alcohol abuse, amphetamines and LSD ingestion by history
McCarron[4]	marijuana smoking and alcohol abuse by history; denied other illicit drugs
Mouzak (1)[5]	marijuana smoking by history and urine toxicology testing; urine was also screened for 11 drugs and was negative (including cocaine, heroin, barbiturates, ethanol, phencyclidine, propoxyphene)
Mouzak (2)[5]	marijuana smoking by history and urine toxicology; no other drugs present on tox screen
Mouzak (3)[5]	marijuana smoking by history and urine toxicology; no other drugs present on tox screen
Marinella[6]	marijuana smoking by history and urine toxicology for cannabinoids
Mesec[7]	marijuana smoking and alcohol abuse by history; urine toxicology confirmed traces of cannabinoids, with no traces of amphetamines or other substances
Alvaro[8]	marijuana smoking by history; denied alcohol or other street drugs
Russmann[9]	marijuana smoking by history and “drug screening for cannabinoids”
Finsterer[10]	marijuana smoking by history; denied amphetamines, ecstasy or any other illicit drugs; he was not screened for opiates, cocaine, cannabinoids, amphetamines or benzodiazepines but patient’s relatives “convincingly confirmed” that he was taking cannabinoids exclusively
Haubrich[11]	marijuana smoking by history
Mateo[12]	hashish consumption by history and urine toxicology; urine screening on admission was negative for amphetamines, cocaine, methadone, opiates, benzodiazepines and barbiturates
Termote[13]	marijuana smoking by history and urine toxicology; the latter was negative for cocaine
Renard[14]	marijuana smoking by history and urine toxicology; the latter was negative for cocaine, heroin and amphetamines
Bal[15]	marijuana smoking by history
Pazderska[16]	marijuana smoking by history and urine toxicology; the latter was positive for both cocaine and cannabis
Reece[17]	marijuana and hashish exposure by history; denied heroin and alcohol use
Giray[18]	hashish exposure by history and laboratory testing (included THC, ethyl alcohol, methyl alcohol, carboxyhemoglobin, pesticides, narcotics and other drugs; THC was the only positive result)
Maguire[19]	marijuana, alcohol, amphetamine, and diazepam exposure by history; urine toxicology was positive for cannabis and benzodiazepines
Trojak[20]	marijuana use by history and urine toxicology; the latter was negative for opioids, cocaine, amphetamines and psychotropic drugs; blood alcohol level was negative

Wolff (1 - 10)[21]	marijuana and other illicit drugs by history and urine screening (cannabinoids, cocaine, amphetamine, methylenedioxymethamphetamine); five patients binged on alcohol
Drumm (1-3)[22]	marijuana use by history
Renard[23]	marijuana use by history and urine toxicology; the latter was negative for cocaine, heroin and amphetamines
Singh (1 - 17)[24]	marijuana use by history and urine toxicology for 11 drugs (including cannabis, cocaine, heroin, barbiturates, ethanol, phencyclidine, amphetamines, LSD, methadone, benzodiazepines, and propoxyphene); no street drug use reported
El Scheich[25]	marijuana use by history and urine toxicology; the latter was negative for other street drugs
Terceno[26]	marijuana use by history
Baharnoori[27]	marijuana use by history; denied other street drugs
Ibrir[28]	marijuana use by history and urine toxicology; the latter was negative for other drugs
Inal[29]	marijuana use by history and urine toxicology (which was negative for benzodiazepines, barbiturates, methamphetamine, cocaine, opioids, phencyclidine and tricyclic antidepressants)
Nouh[30]	marijuana use by history
Oyinloye[31]	marijuana use by history and urine toxicology (which was negative for amphetamines, cocaine, methadone and opiates)
Santos[32]	marijuana use by history and urine toxicology (which was negative for amphetamines, cocaine, and benzodiazepines)
Smaoui[33]	marijuana use by history and urine toxicology
Tsivgoulis[34]	marijuana use by history; other street drugs denied

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