Società Italiana Interdisciplinare NeuroVascolare

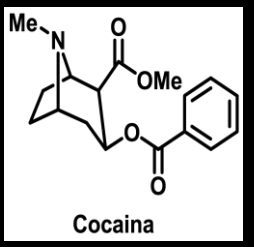
Le Nuove frontiere dell'Ictus

San Benedetto del Tronto 28-29 ottobre 2016

Stroke e cocaina: una realtà emergente

Antonio Siniscalchi
U.O. di Neurologia
Azienda Ospedaliera di Cosenza

LA COCAINA



Cocaina

La cocaina cloridrato è la forma farmaceutica usata come anestetico locale e abusata dai tossicomani per via nasale e/o endovena. Dalla ebollizione della cocaina cloridrato in ambiente alcalino (bicarbonato; baking-soda) si libera la cocaina base che può essere estratta con etere (free-base) o più semplicemente raccolta come una pasta al termine della evaporazione dell'acqua.

La cocaina base, conosciuta come crack , può essere fumata raggiungendo tassi ematici più elevati e più rapidi rispetto all'uso intranasale del cloridrato. Il crack si presenta sotto forma di cristalli di colore azzurrino/biancastro. Lo si assume con apposite pipe di vetro o legno inalando il fumo dopo aver surriscaldato i cristalli. Questa operazione provoca degli scricchiolii che danno origine al suo nome

REVIEW

Cocaine use and stroke

Sean D Treadwell, Tom G Robinson

Postgrad Med J 2007;**83**:389–394. doi: 10.1136/pgmj.2006.055970

Box 1 Clinical manifestations of cocaine use

Cardiac
- Myocardial infarction
- Cardiomyopathy
- Myocarditis
- Arrhythmias
- Sudden death

Pulmonary
- Pneumothorax
- Pneumomediastinum
- Pulmonary oedema
- Pulmonary haemorrhage
- Bronchiolitis obliterans

Psychiatric
- Anxiety/depression
- Paranoia
- Delirium
- Psychosis

Neurology
- Headache
- Seizures
- Stroke
- Cerebral atrophy
- Cerebral vasculitis

Gastrointestinal
- Ischaemic colitis

Head and neck
- Enamel erosion
- Gingival ulceration
- Chronic rhinitis
- Osteolytic sinusitis
- Abnormal olfaction
- Perforated nasal septum
- Midline granuloma

Endocrine
- Gynaecomastia
- Galactorrhoea
- Sexual dysfunction

Infections (in intravenous users)
- Bacterial endocarditis
- HIV
- Hepatitis
- Injection site abscess
- Cellulitis

Other
- Weight loss
- Optic neuropathy
- Rhabdomyolysis
- Arterial/venous thrombosis

Urine toxicology screening in an urban stroke and TIA population

Brian Silver, MD
Daniel Miller, MD
Michelle Jankowski, MAS
Nawaf Murshed, MD
Patricia Garcia, DO
Patricia Penstone, RN
Melissa Straub, MSII
Sean P. Logan, MD
Anita Sinha, MD
Daniel C. Morris, MD
Angelos Katramados, MD
Andrew N. Russman, DO
Panayiotis D. Mitsias, MD, PhD
Lonni R. Schultz, PhD

. *Neurology*® 2013;80:1702-1709

Table 1 Patient characteristics

	All patients	Ischemic stroke	Intracerebral hemorrhage	TIA

A total of 1,024 patients were identified: 704 with ischemic stroke, 133 with intracerebral hemorrhage, and 205 with TIA

Table 2 Performance and results of urine toxicology by age, sex, and race

420 patients (40%)

Age, y	Urine toxicology performed, n/N (%)	p Value[a]	Urine toxicology cocaine-positive, n/N (%)	p Value[a]	Urine toxicology opiate-positive, n/N (%)	p Value[a]
<50	101/140 (72)	<0.001	19/101 (19)	<0.001	19/101 (19)	0.43
50-59	115/211 (55)		22/115 (19)		26/115 (23)	
60-69	91/227 (40)		4/91 (4)		14/91 (20)	
70-79	59/237 (25)		2/59 (3)		8/59 (13)	
≥80	54/227 (24)		0/54 (0)		7/54 (14)	
Sex						
Male	217/502 (43)	0.064	34/217 (16)	0.003	36/217 (17)	0.567
Female	203/540 (38)		13/203 (6)		38/203 (19)	
Race						
Black	311/650 (48)	<0.001	40/311 (13)	0.055	58/311 (19)	0.73
White	82/325 (25)		3/82 (4)		12/82 (15)	
Asian	3/10 (30)		0/3 (0)		0/3 (0)	

[a] Comparisons are across categories, i.e., age, sex, and race.

Ictus e cocaina

La cocaina induce sia un ictus ischemico che emorragico, anche se l'incidenza dell'ictus emorragico e più alta dell'ictus ischemico

Johnson B A et al, 2001; Toosi S et al, 2010; Siniscalchi et al. 2015, 2016

Current Neurovascular Research, 2015, *12*, 163-172

Cocaine Dependence and Stroke: Pathogenesis and Management

Antonio Siniscalchi[1,*], Antonello Bonci[2], Nicola Biagio Mercuri[3], Antonia De Siena[4], Giovambattista De Sarro[5], Giovanni Malferrari[6], Marco Diana[7] and Luca Gallelli[5]

[1]Department of Neuroscience, Neurology Division, "Annunziata" Hospital, Cosenza, Italy; [2]Intramural research program, National Institute on Drug Abuse, NIH, Baltimore, 21224, USA; [3]IRCCS-FondazioneS. Lucia and Department of Neurophysiopathology University "Tor Vergata", Rome, Italy; [4]Dependance Unit, Lamezia Terme Hospital (CZ), Azienda Sanitaria Provinciale CZ, Italy; [5]Department of Health Science, School of Medicine, University Magna Graecia of Catanzaro, Clinical Pharmacology and Pharmacovigilance Unit, Mater Domini University Hospital, Catanzaro, Italy; [6]Department of Neurology, Santa Maria Nuova Hospital, Reggio Emilia, Italy; [7]"G.Minardi" Laboratory of Cognitive Neuroscience, Dept of Chemistry & Pharmacy, University of Sassari, Italy

The use of cocaine is associated with both ischaemic and haemorrhagic stroke. In particular, crack cocaine seems to be associated with both ischemic strokes and hemorrhage strokes, whereas cocaine hydrochloride causes mainly intracerebral and subarachnoidal bleeding [33]. Early studies

2.5. Other Mechanisms in Cocaine – Induced Stroke: Secondary Factors

The mechanism of cocaine related stroke is confounded by contaminants, such as procainamide, quinidine and antihistamines, which are often mixed with the cocaine. These

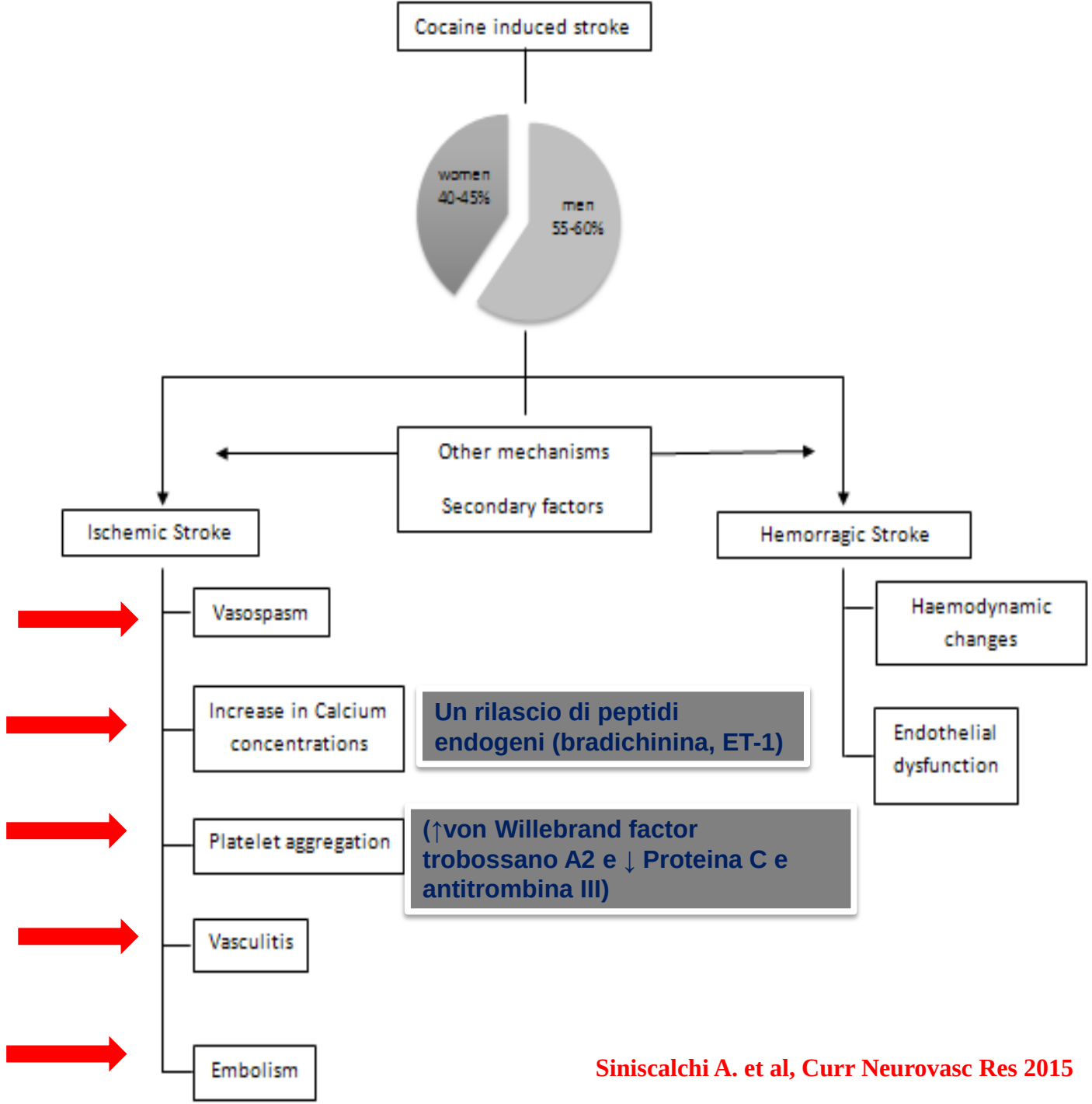
Neurovascular Complications of Cocaine Use at a Tertiary Stroke Center

Shahed Toossi, BA,* Christopher P. Hess, MD, PhD,† Nancy K. Hills, PhD,* and S. Andrew Josephson, MD*

A total of 5142 records, 45 were ischemic stroke and TIA cases were further classified by clinical and radiographic features according to TOAST criteria:

- 20 (44%) large artery atherosclerosis (subtype 1),
- 5 (11%) cardioembolic (subtype 2),
- 10 (22%) small vessel occlusion (subtype 3),
- 4 (9%) stroke of other determined cause (subtype 4),
- and 6 (13%) stroke of other undetermined origin (subtype 5)

Journal of Stroke and Cerebrovascular Diseases, Vol. 19, No. 4 (July–August), 2010: pp 273-278

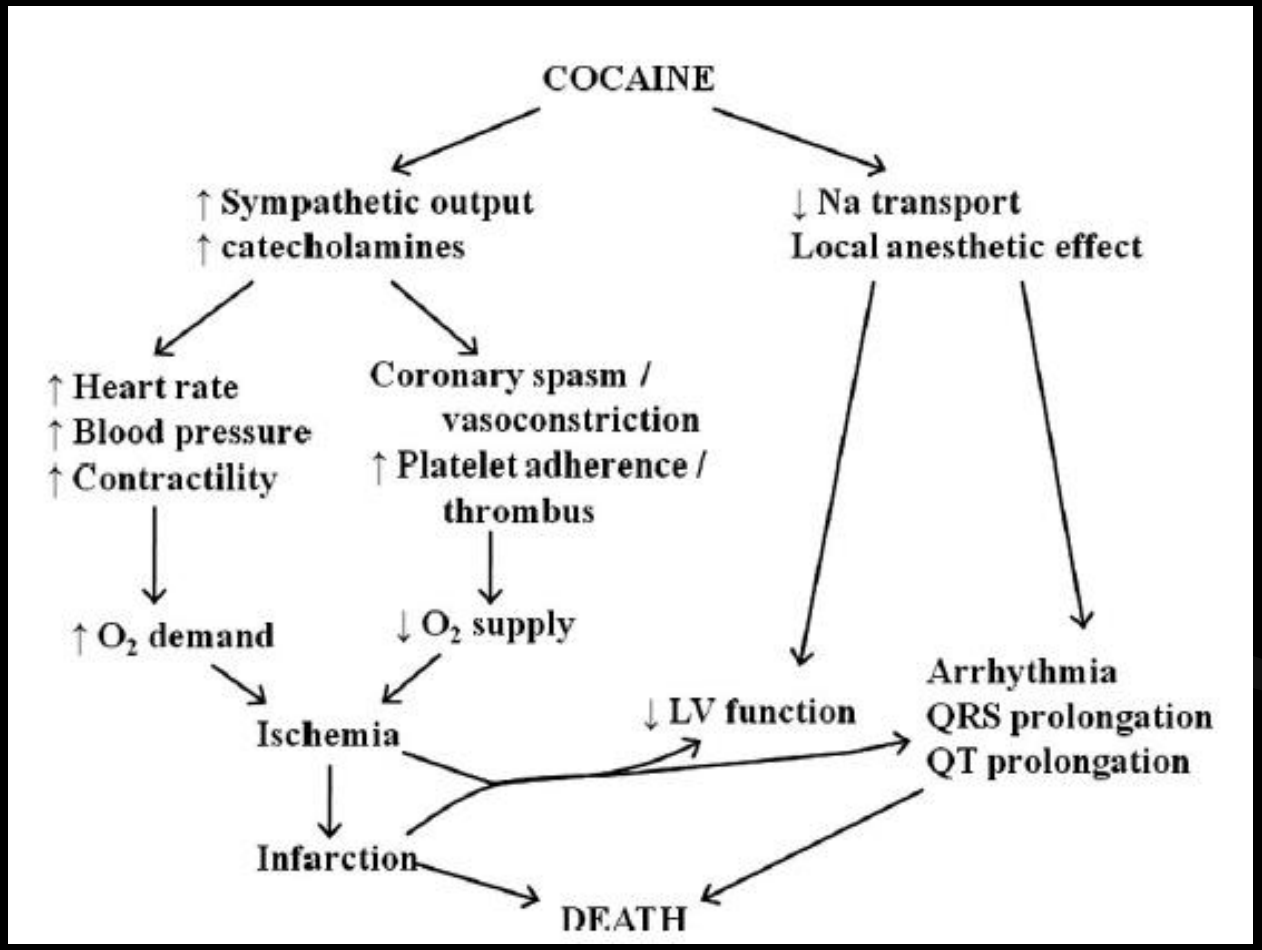


Siniscalchi A. et al, Curr Neurovasc Res 2015

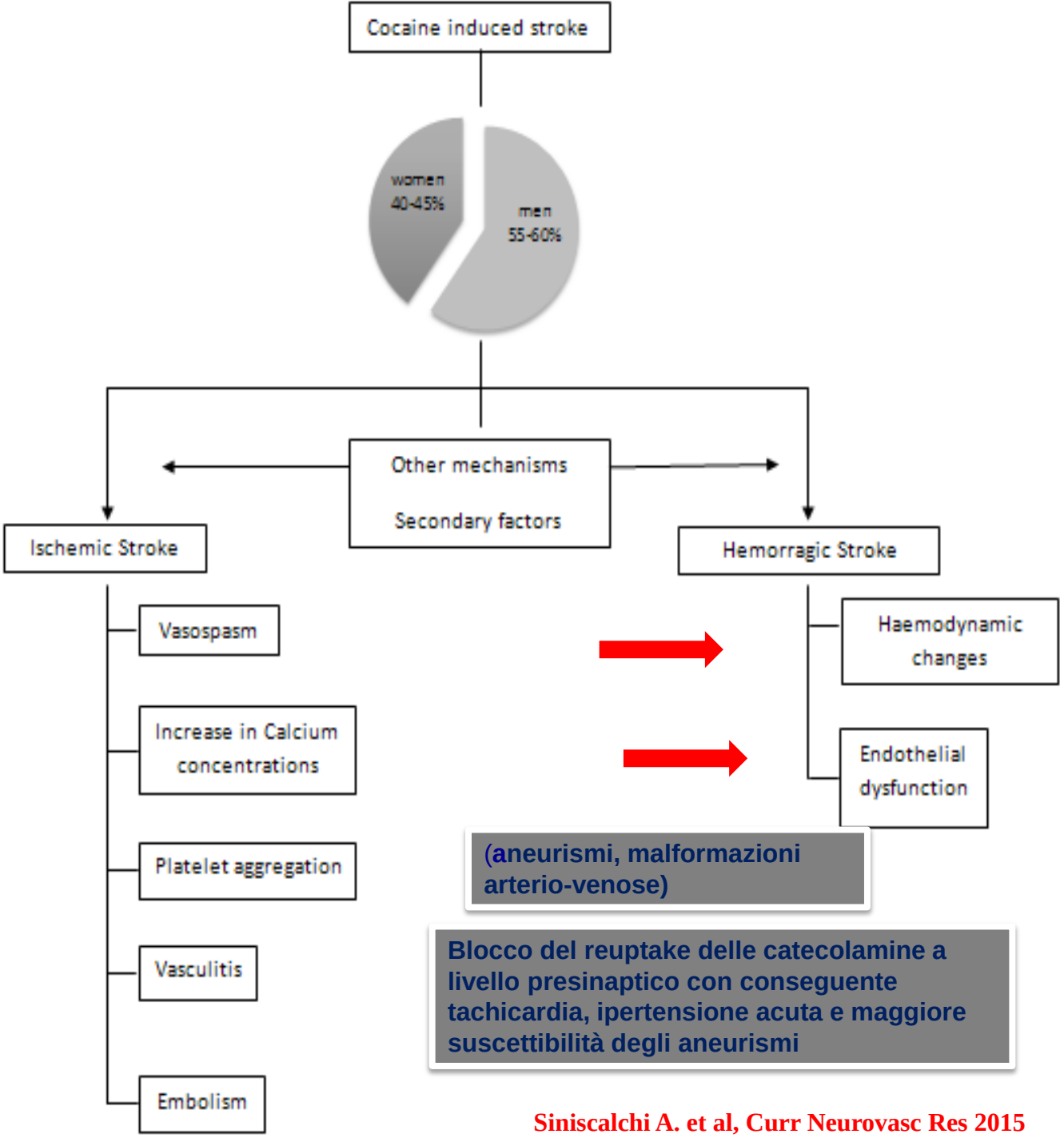
Contemporary Reviews in Cardiovascular Medicine

Cardiovascular Effects of Cocaine

Bryan G. Schwartz, MD; Shereif Rezkalla, MD; Robert A. Kloner, MD, PhD



Circulation. 2010;122:2558-2569



Siniscalchi A. et al, Curr Neurovasc Res 2015

Neurovascular Complications of Cocaine Use at a Tertiary Stroke Center

Shahed Toossi, BA,* Christopher P. Hess, MD, PhD,† Nancy K. Hills, PhD,* and S. Andrew Josephson, MD*

Results

Cocaine-related ICH in this cohort was in typical hypertensive hemorrhage locations including the basal ganglia and thalami

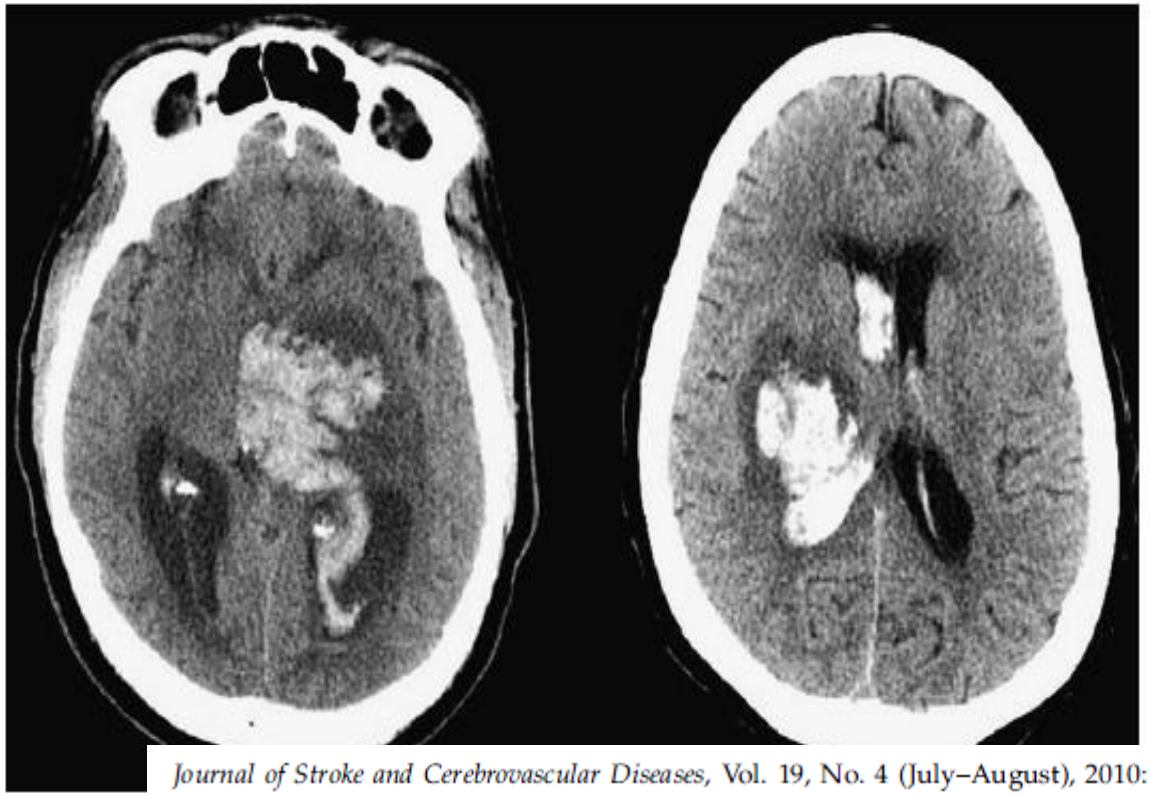


Figure 3. *Hypertensive hemorrhage in an active user of cocaine. Two examples of parenchymal hemorrhage, both in typical locations for hypertensive hemorrhages with decompression into ventricular system. Hemorrhage centered in left thalamus (left) and in the right posterior basal ganglia (right).*

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American Journal of Emergency Medicine xxx (2016) xxx–xxx

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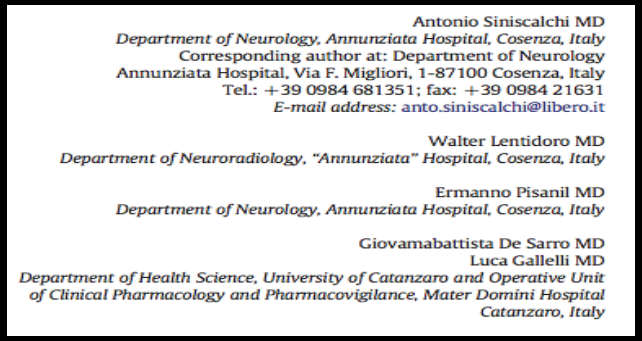
ELSEVIER

Case Report

Intracerebral hemorrhage in a middle-aged cocaine user despite normal blood pressures☆



Antonio Siniscalchi MD
Department of Neurology, Annunziata Hospital, Cosenza, Italy
Corresponding author at: Department of Neurology
Annunziata Hospital, Via F. Migliori, 1-87100 Cosenza, Italy
Tel.: +39 0984 681351; fax: +39 0984 21631
E-mail address: anto.siniscalchi@libero.it

Walter Lentidoro MD
Department of Neuroradiology, "Annunziata" Hospital, Cosenza, Italy

Ermanno Pisanil MD
Department of Neurology, Annunziata Hospital, Cosenza, Italy

Giovamabattista De Sarro MD
Luca Gallelli MD
Department of Health Science, University of Catanzaro and Operative Unit of Clinical Pharmacology and Pharmacovigilance, Mater Domini Hospital Catanzaro, Italy

- A 40-year old woman who did not declare at admission her 4-year history of intranasal cocaine hydrochloride abuse
- presented to our observation in emergency department for facial paralysis on the left side of her body, mild dysarthria, and hemiplegic upper limb and lower limb left, with the positivity to Babinski sign on the left.
- History revealed that she had migraine with vomiting and photophobia in 2013 that resolved with sleep but excluded the presence of other systemic diseases, medical or surgical history, and alcohol abuse.
- Clinical evaluation document ed a normal blood pressure (115/70 mm Hg; heart rate, 85 beats/min).
- We performed a urine toxicology screen test revealing that she was positive for cocaine and lorazepam used (at the final dosage of 1 mg/d) to treat anxiety symptoms. No other drugs were taken by the patient at the time of this study.

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Case Report

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Corresponding author at: Department of Neurology
Annunziata Hospital, Via F. Migliori, 1-87100 Cosenza, Italy
Tel.: +39 0984 681351; fax: +39 0984 21631
E-mail address: anto.siniscalchi@libero.it

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Department of Neuroradiology, "Annunziata" Hospital, Cosenza, Italy

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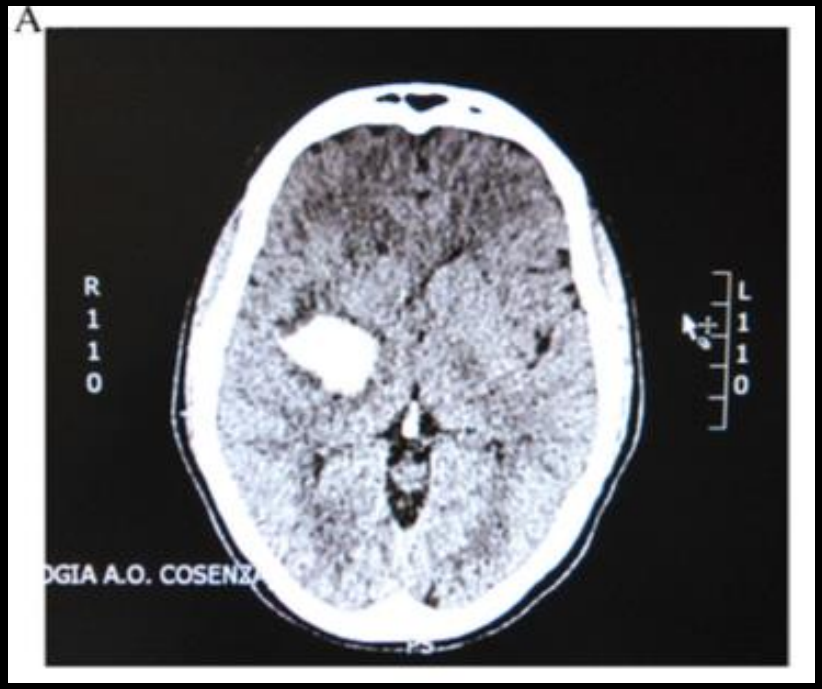


In conclusion, we strongly suggest that a toxicological drug screening test be performed in young patients with normal blood pressure and with spontaneous subcortical hemorrhagic stroke in the presence of negative anamnesis for drug abuse at admission. The mechanisms of cocaine-induced intracerebral hemorrhage in presence of normal blood pressure also require further study.

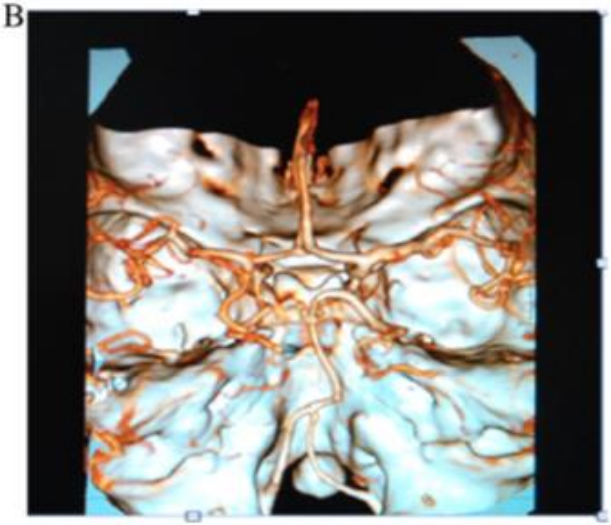


Figure. A, CT scan showing a small right subcortical (right basal ganglia) intracerebral hemorrhage in a cocaine user. B, CT angiography image of the circle of Willis.

ICTUS ISCHEMICO
E
COCAINA

TROMBOLISI

Intravenous Tissue Plasminogen Activator in Patients With Cocaine-Associated Acute Ischemic Stroke

Sheryl Martin-Schild, MD, PhD; Karen C. Albright, DO, MPH; Vivek Misra, MD; Maria Philip, MD; Andrew D. Barreto, MD; Hen Hallevi, MD; James C. Grotta, MD; Sean I. Savitz, MD

Table 1. Comparison of Cocaine-Negative and Cocaine-Positive Patients With Acute Ischemic Stroke Treated With Intravenous tPA

	Cocaine-Negative (N=75)	Cocaine-Positive (N=29)	*P*
Age*	55 (32–91)	48 (19–67)	0.001
Gender, male, %	61.3	82.8	0.039
Race, %			0.423
White	34.7	20.7	
Black	50.7	65.5	
Hispanic	13.3	10.3	
Asian	1.3	3.4	
History of hypertension, %	70.7	67.9	0.782
First systolic blood pressure*	164 (96–223)	166 (101–257)	0.545
First diastolic blood pressure*	89 (63–141)	99 (67–173)	0.022
Glucose*	123 (62–354)	103.5 (81–286)	0.003
Creative kinase*	135 (25–937)	192.5 (43–637)	0.037
CK-MB*	3.1 (0.8–10.5)	3.2 (1.4–67)	0.614
Troponin*	0.01 (0.01–3.84)	0.01 (0.01–2.41)	0.423
sICH	1.3% (1/75)	0% (0/29)	1.000
mRS on discharge*	2.0 (0–6)	2.5 (0–6)	0.612
Favorable mRS on discharge (95% CI)	52.0% (42.3%–61.5%)	50.0% (40.4%–59.6%)	1.000
Favorable disposition (95% CI)	72.0% (62.6%–79.9)	82.8% (74.4%–89.2%)	0.319
Death (95% CI)	12.0% (9%–20%)	3.4% (0.7%–8.8%)	0.276
Baseline NIHSS*	11 (3–35)	13 (4–23)	0.777
Time to intravenous tPA, minutes*	141 (65–180)	116.5 (69–173)	0.201

*Median (minimum–maximum).

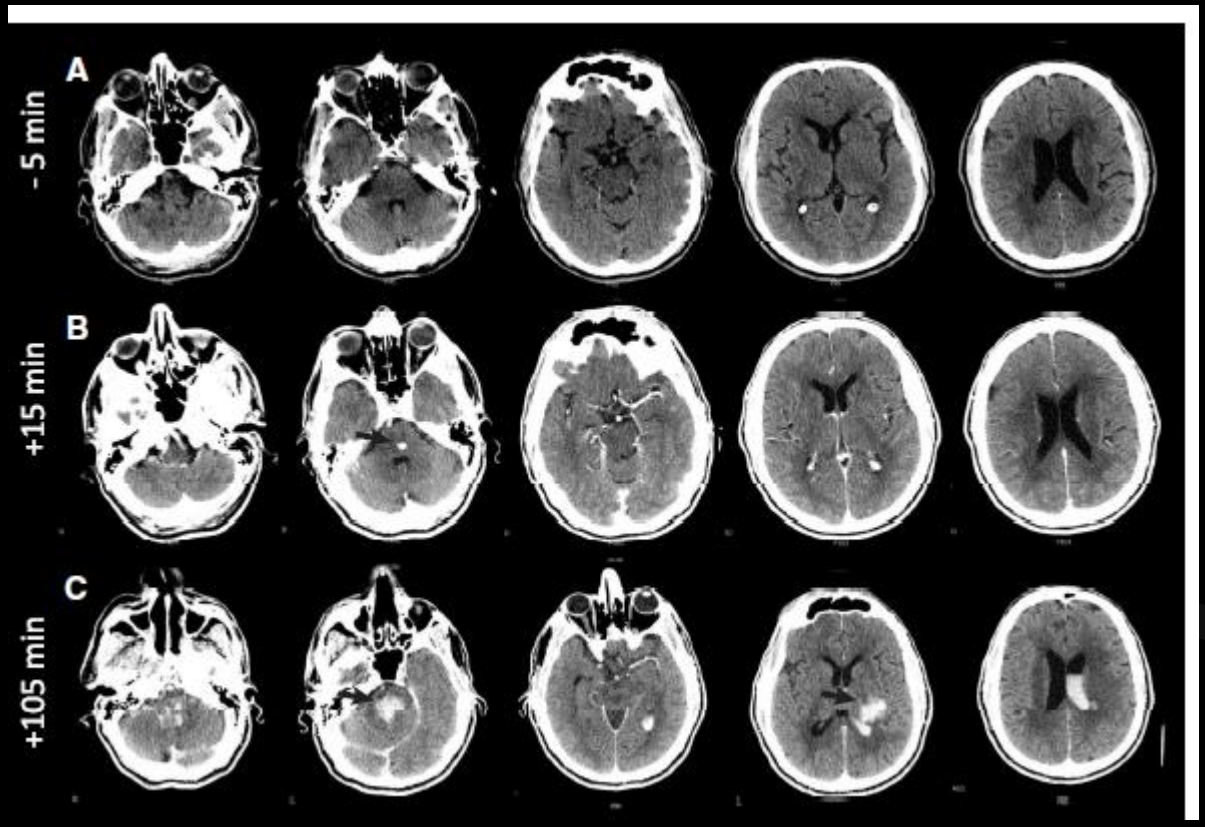
(*Stroke*. 2009;40:3635-3637.)

Illustrative Teaching Cases

Section Editors: Daniel Strbian, MD, PhD, and Sophia Sundararajan, MD, PhD

Immediate Hemorrhagic Transformation After Intravenous Tissue-Type Plasminogen Activator Injection in 2 Cocaine Users

Maxime O. Baud, MD, PhD*; Ethan G. Brown, MD*; Neel S. Singhal, MD, PhD; J. Claude Hemphill III, MD, MAS



Stroke. 2015 Jul;46(7):e167-9.

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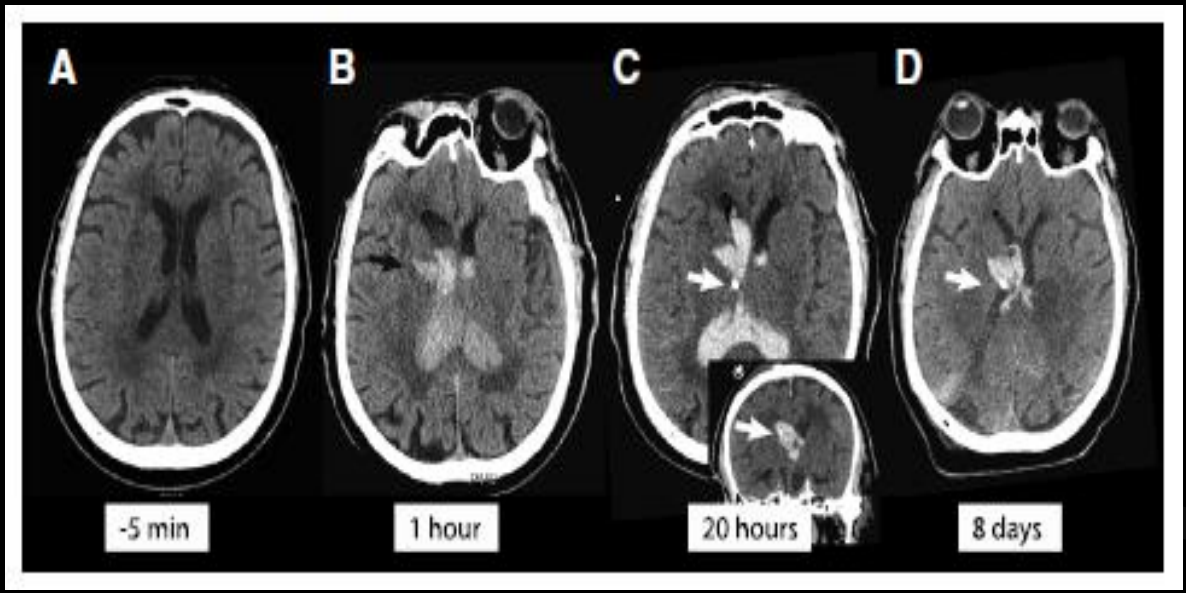


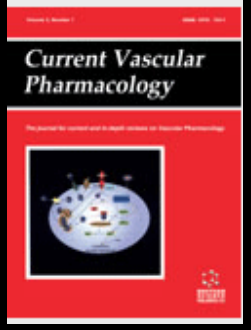
Stroke. 2015 Jul;46(7):e167-9.

Editorial

Cocaine and Cerebral Small Vessel: Is it a Negative Factor for Intravenous Thrombolysis?

Antonio Siniscalchi[1,*], Roman Sztajzel[2], Antonello Bonci[3], Giovanni Malferrari[4], Giovambattista De Sarro[5] and Luca Gallelli[5]

[1]*"Annunziata" Hospital", - Department of Neurology, Cosenza, Italy;* [2]*Department of Neurology, University Hospital of Geneva, Switzerland;* [3]*Intramural research program, National Institute on Drug Abuse, NIH, Baltimore, 21224, USA;* [4]*Department of Neurology, Santa Maria Nuova Hospital, Reggio Emilia, Italy;* [5]*University of Catanzaro, Clinical Pharmacology Unit, Mater Domini University Hospital - Chair of Pharmacology, Department of Health Science, School of Medicine, Catanzaro, Italy*



- The risk of hemorrhagic transformation of ischemic stroke increases by 10-fold after thrombolysis and recognized risk factors include hyperglycemia, high National Institutes of Health Stroke Scale score and the use of antiplatelet agents none of which were present in these two patients. Hypertensive surges are also postulated as a potential mechanism for increased risk of ICH with cocaine but were not present in these patients.

- A recent studies reported that thrombolysis is an effective treatment in acute lacunar stroke, and that the presence of cerebral small vessel disease increases the risk of ICH during thrombolysis even if it does not represent an absolute exclusion criterion
- Small-vessel ischemic disease is often due to hypertension; however, other hypotheses have been suggested including blood-brain barrier alterations, chronic brain edema and genetic factors. Genetic factors for small-vessel ischemic disease include the expression of apolipoprotein E, homozygous methylene tetrahydrofolate reductase 677TT and angiotensin-converting enzyme D/D genotypes and NOTCH-3.

Editorial

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- In addition, the genetic factors for small-vessel ischemic disease may influence the high-risk of ICH in cocaine-users undergoing intravenous thrombolysis.
- An experimental study reported that tPA modulates the biochemical response to cocaine and acute cocaine exposure increases extracellular tPA activity . tPA initiates fibrinolysis and a dysfunction of the tPA inhibitor (PAI-1) results in recurrent hemorrhages .

- Prospective clinical trials may be useful in order to confirm these ob servations reported by Baud *et al.* and to better determine whether intravenous tPA, in the presence of the cerebral small vessel represents an increased risk of ICH in cocaine users.

Take home message

STROKE E COCAINA

- La cocaina è un importante fattore di rischio per entrambi ictus ischemici ed emorragici nei giovani adulti.
- E'utile eseguire uno screenig tossicologico nelle urine, in particolare nei pazienti giovani di sesso maschile senza apparenti tradizionali fattori di rischio
- La maggior parte dell'ictus emorragico ha una localizzazione sottocorticale , un maggiore rischio di inondazione ventricolare e una prognosi peggiore e può non essere associato ad ipertensione arteriosa
- Il trattamento con trombolisi endovenosa sembra non determinare un incremento delle complicanze emorragiche, nè una peggiore prognosi, nè una maggiore mortalità
- Nella trombolisi endovenosa, una maggiore attenzione è necessaria nei pazienti che fanno uso cronico di cocaina ed in presenza di leucoaraiosi alle neuroimmagini.


Grazie per l'attenzione