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Migraine and brain lesions. Data from the population-based CAMERA Study

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ABBREVIATIONS

AICA	anterior inferior cerebellar artery	ILL	infarct-like lesion
ANS	autonomic nervous system	MA	migraine with aura
BBB	blood brain barrier	MO	migraine without aura
BMI	body mass index	MRI	magnetic resonance imaging
BP	blood pressure	OC	oral contraceptives
CAMERA	Cerebral Abnormalities in Migraine, an Epidemiological Risk Analysis	OH	orthostatic hypotension
CI	confidence interval	OI	orthostatic insufficiency
CSD	cortical spreading depression	OR	odds ratio
CSF	cerebro-spinal fluid	PAG	periaqueductal grey matter
CSM	carotid sinus massage	PC / PCT	posterior circulation territory
CT	computed tomography	PD	proton density
DLB	dementia wit Lewy bodies	PFO	patent foramen ovale
DWML	deep white matter lesion	PHL	pontine hyperintense lesion
FLAIR	fluid-attenuated inversion recovery	PICA	posterior inferior cerebellar artery
GEM	genetic epidemiology of migraine	POTS	postural tachycardia syndrome
ICC	intraclass correlation coefficients	PVWML	periventricular white matter lesion
IHL	infratentorial hyperintense lesion	rCBF	regional cerebral blood flow
IHS	international headache society	RR	relative risk
		SCA	superior cerebellar artery
		SN	substantia nigra
		TIA	transient ischemic attack
		WML	white matter hyperintense lesions

DIAGNOSTIC CRITERIA – ICHD-II

The International Classification of Headache Disorders, 2nd edition³

1. MIGRAINE

- 1.1 Migraine without aura
- 1.2 Migraine with aura
 - 1.2.1 Typical aura with migraine headache
 - 1.2.2 Typical aura with non-migraine headache
 - 1.2.3 Typical aura without headache
 - 1.2.4 Familial hemiplegic migraine (FHM)
 - 1.2.5 Sporadic hemiplegic migraine
 - 1.2.6 Basilar-type migraine
- 1.3 Childhood periodic syndromes that are commonly precursors of migraine
 - 1.3.1 Cyclical vomiting
 - 1.3.2 Abdominal migraine
 - 1.3.3 Benign paroxysmal vertigo of childhood
- 1.4 Retinal migraine
- 1.5 Complications of migraine
 - 1.5.1 Chronic migraine
 - 1.5.2 Status migrainosus
 - 1.5.3 Persistent aura without infarction
 - 1.5.4 Migrainous infarction
 - 1.5.5 Migraine-triggered seizure
- 1.6 Probable migraine
 - 1.6.1 Probable migraine without aura
 - 1.6.2 Probable migraine with aura
 - 1.6.5 Probable chronic migraine

1.1 MIGRAINE WITHOUT AURA

Previously used terms:

Common migraine, hemicrania simplex

Description:

Recurrent headache disorder manifesting in attacks lasting 4–72 hours. Typical characteristics of the headache are unilateral location, pulsating quality, moderate or severe intensity, aggravation by routine physical activity and association with nausea and/or photophobia and phonophobia.

Diagnostic criteria:

- A. At least 5 attacks fulfilling criteria B–D
- B. Headache attacks lasting 4–72 hours (untreated or unsuccessfully treated)
- C. Headache has at least two of the following characteristics:
 - 1. unilateral location
 - 2. pulsating quality
 - 3. moderate or severe pain intensity
 - 4. aggravation by or causing avoidance of routine physical activity (e.g., walking or climbing stairs)
- D. During headache at least one of the following:
 - 1. nausea and/or vomiting
 - 2. photophobia and phonophobia
- E. Not attributed to another disorder

1.2 MIGRAINE WITH AURA

Previously used terms:

Classic or classical migraine, ophthalmic, hemiparaesthetic, hemiplegic or aphasic migraine, migraine accompagnée, complicated migraine

Description:

Recurrent disorder manifesting in attacks of reversible focal neurological symptoms that usually develop gradually over 5–20 minutes and last for less than 60 minutes. Headache with the features of migraine without aura usually follows the aura symptoms. Less commonly, headache lacks migrainous features or is completely absent.

Diagnostic criteria:

- A. At least 2 attacks fulfilling criterion B
- B. Migraine aura fulfilling criteria B and C for one of the subforms 1.2.1–1.2.6
- C. Not attributed to another disorder

1.2.1 TYPICAL AURA WITH MIGRAINE HEADACHE

Description:

Typical aura consisting of visual and/or sensory and/or speech symptoms. Gradual development, duration no longer than one hour, a mix of positive and negative features and complete reversibility characterise the aura which is associated with a headache fulfilling criteria for 1.1 Migraine without aura.

Diagnostic criteria:

- A. At least 2 attacks fulfilling criteria B–D
- B. Aura consisting of at least one of the following, but no motor weakness:
 - 1. fully reversible visual symptoms including positive features (*e.g.*, flickering lights, spots or lines) and/or negative features (*i.e.*, loss of vision)
 - 2. fully reversible sensory symptoms including positive features (*i.e.*, pins and needles) and/or negative features (*i.e.*, numbness)
 - 3. fully reversible dysphasic speech disturbance
- C. At least two of the following:
 - 1. homonymous visual symptoms¹ and/or unilateral sensory symptoms
 - 2. at least one aura symptom develops gradually over ≥ 5 minutes and/or different aura symptoms occur in succession over ≥ 5 minutes
 - 3. each symptom lasts ≥ 5 and ≤ 60 minutes
- D. Headache fulfilling criteria B–D for 1.1 Migraine without aura begins during the aura or follows aura within 60 minutes
- E. Not attributed to another disorder

REFERENCES

1. migraine. Dictionary.com - Online Etymology Dictionary. Douglas Harper, Historian. <http://dictionary.reference.com/browse/migraine> (accessed: April 29, 2008).
2. Headache Classification Committee of the International Headache Society. Classification and diagnostic criteria for headache disorders, cranial neuralgias and facial pain. *Cephalalgia* 1988;8 Suppl 7:1-96.
3. Headache Classification Subcommittee of the International Headache Society. The International Classification of Headache Disorders: 2nd edition. *Cephalalgia* 2004;24 Suppl 1:9-160.
4. Goadsby PJ, Lipton RB, Ferrari MD. Migraine--current understanding and treatment. *N.Engl.J.Med.* 2002;346(4):257-70.
5. Ferrari MD. Migraine. *Lancet* 1998;351(9108):1043-51.
6. Russell MB, Olesen J. A nosographic analysis of the migraine aura in a general population. *Brain* 1996;119(Pt 2):355-61.
7. Launer LJ, Terwindt GM, Ferrari MD. The prevalence and characteristics of migraine in a population-based cohort: the GEM study. *Neurology* 1999;53(3):537-42.
8. Rasmussen BK. Epidemiology of headache. *Cephalalgia* 2001;21(7):774-7.
9. Lipton RB, Scher AI, Kolodner K, Liberman J, Steiner TJ, Stewart WF. Migraine in the United States: epidemiology and patterns of health care use. *Neurology* 2002;58(6):885-94.
10. Stewart WF, Lipton RB, Celentano DD, Reed ML. Prevalence of migraine headache in the United States. Relation to age, income, race, and other sociodemographic factors. *Jama* 1992;267(1):64-9.
11. Lipton RB, Bigal ME, Diamond M, Freitag F, Reed ML, Stewart WF. Migraine prevalence, disease burden, and the need for preventive therapy. *Neurology* 2007;68(5):343-9.
12. Leonardi M, Steiner TJ, Scher AT, Lipton RB. The global burden of migraine: measuring disability in headache disorders with WHO's Classification of Functioning, Disability and Health (ICF). *J.Headache Pain* 2005;6(6):429-40.
13. Hu XH, Markson LE, Lipton RB, Stewart WF, Berger ML. Burden of migraine in the United States: disability and economic costs. *Arch.Intern.Med.* 1999;159(8):813-8.
14. Berg J, Stovner LJ. Cost of migraine and other headaches in Europe. *Eur.J.Neurol.* 2005;12 Suppl 1:59-62.
15. Goadsby PJ. Migraine pathophysiology. *Headache* 2005;45 Suppl 1:S14-S24.
16. Colson NJ, Lea RA, Quinlan S, Griffiths LR. The role of vascular and hormonal genes in migraine susceptibility. *Mol.Genet.Metab* 2006;88(2):107-13.
17. Pietrobon D, Striessnig J. Neurobiology of migraine. *Nat.Rev.Neurosci.* 2003;4(5):386-98.
18. Weiller C, May A, Limmroth V, Juptner M, Kaube H, Schayck RV et al. Brain stem activation in spontaneous human migraine attacks. *Nat Med* 1995;1(7):658-60.
19. Moskowitz MA, Bolay H, Dalkara T. Deciphering migraine mechanisms: clues from familial hemiplegic migraine genotypes. *Ann.Neurol.* 2004;55(2):276-80.
20. Aurora SK, Welch KM. Migraine: imaging the aura. *Curr.Opin.Neurol.* 2000;13(3):273-6.
21. Cao Y, Welch KM, Aurora S, Vikingstad EM. Functional MRI-BOLD of visually triggered headache in patients with migraine. *Archives of Neurology* 1999;56(5):548-54.
22. Welch KM, Cao Y, Aurora S, Wiggins G, Vikingstad EM. MRI of the occipital cortex, red nucleus, and substantia nigra during visual aura of migraine. *Neurology* 1998;51(5):1465-9.
23. Smith JM, Bradley DP, James MF, Huang CL. Physiological studies of cortical spreading depression. *Biol.Rev.Camb.Philos.Soc.* 2006;81(4):457-81.
24. Takano T, Tian GF, Peng W, Lou N, Lovatt D, Hansen AJ et al. Cortical spreading depression causes and coincides with tissue hypoxia. *Nat.Neurosci.* 2007;10(6):754-62.
25. GURSOY-OZDEMIR Y, QIU J, MATSUOKA N, BOLAY H, BERMPHOHL D, JIN H et al. Cortical spreading depression activates and upregulates MMP-9. *J.Clin.Invest* 2004;113(10):1447-55.

26. Cutrer FM, O'Donnell A, Sanchez dR. Functional neuroimaging: enhanced understanding of migraine pathophysiology. *Neurology* 2000;55(9 Suppl 2):S36-S45.
27. Smith M, Cros D, Sheen V. Hyperperfusion with vasogenic leakage by fMRI in migraine with prolonged aura. *Neurology* 2002;58(8):1308-10.
28. Resnick S, Reyes-Iglesias Y, Carreras R, Villalobos E. Migraine with aura associated with reversible MRI abnormalities. *Neurology* 2006;66(6):946-7.
29. Liang Y, Scott TF. Migrainous infarction with appearance of laminar necrosis on MRI. *Clin.Neurol.Neurosurg.* 2007;109(7):592-6.
30. Lindner A, Reiners K, Toyka KV. Meningeal hyperperfusion visualized by MRI in a patient with visual hallucinations and migraine. *Headache* 1996;36(1):53-7.
31. Crawford JS, Konkol RJ. Familial hemiplegic migraine with crossed cerebellar diaschisis and unilateral meningeal enhancement. *Headache* 1997;37(9):590-3.
32. Arnold G, Reuter U, Kinze S, Wolf T, Einhaupl KM. Migraine with aura shows gadolinium enhancement which is reversed following prophylactic treatment. *Cephalalgia* 1998;18(9):644-6.
33. Barbour PJ, Castaldo JE, Shoemaker EI. Hemiplegic migraine during pregnancy: unusual magnetic resonance appearance with SPECT scan correlation. *Headache* 2001;41(3):310-6.
34. Dreier JP, Jurkat-Rott K, Petzold GC, Tomkins O, Klingebiel R, Kopp UA et al. Opening of the blood-brain barrier preceding cortical edema in a severe attack of FHM type II. *Neurology* 2005;64(12):2145-7.
35. Iizuka T, Sakai F, Suzuki K, Igarashi H, Suzuki N. Implication of augmented vasogenic leakage in the mechanism of persistent aura in sporadic hemiplegic migraine. *Cephalalgia* 2006;26(3):332-5.
36. van den Maagdenberg AM, Haan J, Terwindt GM, Ferrari MD. Migraine: gene mutations and functional consequences. *Curr.Opin.Neurol.* 2007;20(3):299-305.
37. Aurora SK, Wilkinson F. The brain is hyperexcitable in migraine. *Cephalalgia* 2007;27(12):1442-53.
38. Ebner TJ, Chen G. Spreading acidification and depression in the cerebellar cortex. *Neuroscientist.* 2003;9(1):37-45.
39. Bolay H, Reuter U, Dunn AK, Huang Z, Boas DA, Moskowitz MA. Intrinsic brain activity triggers trigeminal meningeal afferents in a migraine model. *Nat.Med.* 2002;8(2):136-42.
40. Goadsby PJ. Migraine, aura, and cortical spreading depression: why are we still talking about it? *Ann.Neurol.* 2001;49(1):4-6.
41. Dalkara T, Zervas NT, Moskowitz MA. From spreading depression to the trigeminovascular system. *Neurol.Sci.* 2006;27 Suppl 2:S86-S90.
42. Woods RP, Iacoboni M, Mazziotta JC. Brief report: bilateral spreading cerebral hypoperfusion during spontaneous migraine headache. *N Engl J Med* 1994;331(25):1689-92.
43. Cao Y, Aurora SK, Nagesh V, Patel SC, Welch KM. Functional MRI-BOLD of brainstem structures during visually triggered migraine. *Neurology* 2002;59(1):72-8.
44. Sanchez-Del-Rio M, Reuter U, Moskowitz MA. New insights into migraine pathophysiology. *Curr.Opin.Neurol.* 2006;19(3):294-8.
45. Henrich JB, Sandercock PA, Warlow CP, Jones LN. Stroke and migraine in the Oxfordshire Community Stroke Project. *Journal of Neurology* 1986;233(5):257-62.
46. Bogousslavsky J, Regli F, Van Melle G, Payot M, Uske A. Migraine stroke. *Neurology* 1988;38(2):223-7.
47. Rothrock JF, Walicke P, Swenson MR, Lyden PD, Logan WR. Migrainous stroke. *Arch.Neurol.* 1988;45(1):63-7.
48. Sacquegna T, Andreoli A, Baldrati A, Lamieri C, Guttman S, de Carolis P et al. Ischemic stroke in young adults: the relevance of migrainous infarction. *Cephalalgia* 1989;9(4):255-8.
49. Rothrock J, North J, Madden K, Lyden P, Fleck P, Dittrich H. Migraine and migrainous stroke: risk factors and prognosis. *Neurology* 1993;43(12):2473-6.
50. Sochurkova D, Moreau T, Lemesle M, Menassa M, Giroud M, Dumas R. Migraine history and migraine-induced stroke in the Dijon stroke registry. *Neuroepidemiology* 1999;18(2):85-91.
51. Donaghy M, Chang CL, Poulter N. Duration, frequency, recency, and type of migraine and the risk of ischaemic stroke in women of childbearing age. *J. Neurol. Neurosurg. Psychiatry* 2002;73(6):747-50.
52. Schwaag S, Nabavi DG, Frese A, Husstedt IW, Evers S. The association between migraine and juvenile stroke: a case-control study. *Headache* 2003;43(2):90-5.

53. Lidegaard O. Oral contraceptives, pregnancy and the risk of cerebral thromboembolism: the influence of diabetes, hypertension, migraine and previous thrombotic disease. *Br.J Obstet.Gynaecol.* 1995;102(2):153-9.
54. Collaborative Group for the Study of Stroke in Young Women. Oral contraceptives and stroke in young women. Associated risk factors. *Jama* 1975;231(7):718-22.
55. Henrich JB, Horwitz RI. A controlled study of ischemic stroke risk in migraine patients. *J Clin.Epidemiol* 1989;42(8):773-80.
56. Marini C, Carolei A, Roberts RS, Prencipe M, Gandolfo C, Inzitari D et al. Focal cerebral ischemia in young adults: a collaborative case-control study. The National Research Council Study Group. *Neuroepidemiology* 1993;12(2):70-81.
57. Tzourio C, Iglesias S, Hubert JB, Visy JM, Alperovitch A, Tehindrazanarivelo A et al. Migraine and risk of ischaemic stroke: a case-control study. *Bmj* 1993;307(6899):289-92.
58. Tzourio C, Tehindrazanarivelo A, Iglesias S, Alperovitch A, Chedru F, d'Anglejan-Chatillon J et al. Case-control study of migraine and risk of ischaemic stroke in young women. *Bmj* 1995;310(6983):830-3.
59. Carolei A, Marini C, De Matteis G. History of migraine and risk of cerebral ischaemia in young adults. The Italian National Research Council Study Group on Stroke in the Young. *Lancet* 1996;347(9014):1503-6.
60. Buring JE, Hebert P, Romero J, Kittross A, Cook N, Manson J et al. Migraine and subsequent risk of stroke in the Physicians' Health Study. *Arch.Neurol.* 1995;52(2):129-34.
61. Merikangas KR, Fenton BT, Cheng SH, Stolar MJ, Risch N. Association between migraine and stroke in a large-scale epidemiological study of the United States. *Archives of Neurology* 1997;54(4):362-8.
62. Chang CL, Donaghy M, Poulter N. Migraine and stroke in young women: case-control study. The World Health Organisation Collaborative Study of Cardiovascular Disease and Steroid Hormone Contraception. *Bmj* 1999;318(7175):13-8.
63. Haapaniemi H, Hillbom M, Juvela S. Lifestyle-associated risk factors for acute brain infarction among persons of working age. *Stroke* 1997;28(1):26-30.
64. Nightingale AL, Farmer RD. Ischemic stroke in young women: a nested case-control study using the UK General Practice Research Database. *Stroke* 2004;35(7):1574-8.
65. Etminan M, Takkouche B, Isorna FC, Samii A. Risk of ischaemic stroke in people with migraine: systematic review and meta-analysis of observational studies. *Bmj* 2005;330(7482):63.
66. Rovaris M, Bozzali M, Rocca MA, Colombo B, Filippi M. An MR study of tissue damage in the cervical cord of patients with migraine. *J.Neurol.Sci.* 2001;183(1):43-6.
67. Igarashi H, Sakai F, Kan S, Okada J, Tazaki Y. Magnetic resonance imaging of the brain in patients with migraine. *Cephalalgia* 1991;11(2):69-74.
68. Robbins L, Friedman H. MRI in migraineurs. *Headache* 1992;32(10):507-8.
69. Pavese N, Canapicchi R, Nuti A, Bibbiani F, Lucetti C, Collavoli P et al. White matter MRI hyperintensities in a hundred and twenty-nine consecutive migraine patients. *Cephalalgia* 1994;14(5):342-5.
70. De Benedittis G, Lorenzetti A, Sina C, Bernasconi V. Magnetic resonance imaging in migraine and tension-type headache. *Headache* 1995;35(5):264-8.
71. Kruit MC, van Buchem MA, Hofman PA, Bakkers JT, Terwindt GM, Ferrari MD et al. Migraine as a risk factor for subclinical brain lesions. *Jama* 2004;291(4):427-34.
72. Welch KM, Nagesh V, Aurora SK, Gelman N. Periaqueductal gray matter dysfunction in migraine: cause or the burden of illness? *Headache* 2001;41(7):629-37.
73. Welch KM. Relationship of stroke and migraine. *Neurology* 1994;44(suppl 7)(10):S33-6.
74. Tietjen GE. The relationship of migraine and stroke. *Neuroepidemiology* 2000;19(1):13-9.
75. Tzourio C, Kittner SJ, Bousser MG, Alperovitch A. Migraine and stroke in young women. *Cephalalgia* 2000;20(3):190-9.
76. Bousser MG. Estrogens, migraine, and stroke. *Stroke* 2004;35(11 Suppl 1):2652-6.
77. Broderick JP, Swanson JW. Migraine-related strokes. Clinical profile and prognosis in 20 patients. *Archives of Neurology* 1987;44(8):868-71.
78. van den Boom R, Lesnik Oberstein SA, Ferrari MD, Haan J, van Buchem MA. Cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy: MR imaging findings at different ages--3rd-6th decades. *Radiology* 2003;229(3):683-90.

79. Tietjen GE, Al Qasbi MM, Athanas K, Dafer RM, Khuder SA. Increased von Willebrand factor in migraine. *Neurology* 2001;57(2):334-6.
80. Sztajzel R, Genoud D, Roth S, Mermillod B, Floch-Rohr J. Patent foramen ovale, a possible cause of symptomatic migraine: a study of 74 patients with acute ischemic stroke. *Cerebrovasc.Dis.* 2002;13(2):102-6.
81. Heckmann JG, Lang CJ, Dietrich W, Neidhardt B, Neundorfer B. Symptomatic migraine linked to stroke due to paradoxical embolism and elevated thrombosis risk. *Cephalalgia* 2002;22(2):154-6.
82. Klopstock T, May A, Seibel P, Papagiannuli E, Diener HC, Reichmann H. Mitochondrial DNA in migraine with aura. *Neurology* 1996;46(6):1735-8.
83. Shuaib A. Stroke from other etiologies masquerading as migraine-stroke. *Stroke* 1991;22(8):1068-74.
84. Olesen J, Friberg L, Olsen TS, Andersen AR, Lassen NA, Hansen PE et al. Ischaemia-induced (symptomatic) migraine attacks may be more frequent than migraine-induced ischaemic insults. *Brain* 1993;116(Pt 1):187-202.
85. Tzourio C, Benslamia L, Guillon B, Aidi S, Bertrand M, Berthet K et al. Migraine and the risk of cervical artery dissection: a case-control study. *Neurology* 2002;59(3):435-7.
86. Milhaud D, Bogousslavsky J, Van Melle G, Liot P. Ischemic stroke and active migraine. *Neurology* 2001;57(10):1805-11.
87. Hoekstra-van Dalen RA, Cillessen JP, Kappelle LJ, van Gijn J. Cerebral infarcts associated with migraine: clinical features, risk factors and follow-up. *J.Neurol.* 1996;243(7):511-5.
88. WHO Collaborative Study of Cardiovascular Disease and Steroid Hormone Contraception. Ischaemic stroke and combined oral contraceptives: results of an international, multicentre, case-control study. WHO Collaborative Study of Cardiovascular Disease and Steroid Hormone Contraception. *Lancet* 1996;348(9026):498-505.
89. Kase CS, Wolf PA, Chodosh EH, Zacker HB, Kelly-Hayes M, Kannel WB et al. Prevalence of silent stroke in patients presenting with initial stroke: the Framingham Study. *Stroke* 1989;20(7):850-2.
90. Vermeer SE, Prins ND, den Heijer T, Hofman A, Koudstaal PJ, Breteler MM. Silent brain infarcts and the risk of dementia and cognitive decline. *N.Engl.J.Med.* 2003;348(13):1215-22.
91. Bernick C, Kuller L, Dulberg C, Longstreth WT, Jr., Manolio T, Beauchamp N et al. Silent MRI infarcts and the risk of future stroke: the cardiovascular health study. *Neurology* 2001;57(7):1222-9.
92. Vermeer SE, Hollander M, van Dijk EJ, Hofman A, Koudstaal PJ, Breteler MM. Silent brain infarcts and white matter lesions increase stroke risk in the general population: the Rotterdam Scan Study. *Stroke* 2003;34(5):1126-9.
93. Howard G, Wagenknecht LE, Cai J, Cooper L, Kraut MA, Toole JF. Cigarette smoking and other risk factors for silent cerebral infarction in the general population. *Stroke* 1998;29(5):913-7.
94. Bryan RN, Cai J, Burke G, Hutchinson RG, Liao D, Toole JF et al. Prevalence and anatomic characteristics of infarct-like lesions on MR images of middle-aged adults: the atherosclerosis risk in communities study. *AJNR Am J Neuroradiol* 1999;20(7):1273-80.
95. Liao D, Cooper L, Cai J, Toole J, Bryan N, Burke G et al. The prevalence and severity of white matter lesions, their relationship with age, ethnicity, gender, and cardiovascular disease risk factors: the ARIC Study. *Neuroepidemiology* 1997;16(3):149-62.
96. Breteler MM, van Swieten JC, Bots ML, Grobbee DE, Claus JJ, van d et al. Cerebral white matter lesions, vascular risk factors, and cognitive function in a population-based study: the Rotterdam Study. *Neurology* 1994;44(7):1246-52.
97. Longstreth WT, Jr., Manolio TA, Arnold A, Burke GL, Bryan N, Jungreis CA et al. Clinical correlates of white matter findings on cranial magnetic resonance imaging of 3301 elderly people. The Cardiovascular Health Study. *Stroke* 1996;27(8):1274-82.
98. Kuller LH, Longstreth WT, Jr., Arnold AM, Bernick C, Bryan RN, Beauchamp NJ, Jr. White matter hyperintensity on cranial magnetic resonance imaging: a predictor of stroke. *Stroke* 2004;35(8):1821-5.
99. Pantoni L, Garcia JH, Gutierrez JA. Cerebral white matter is highly vulnerable to ischemia. *Stroke* 1996;27(9):1641-6.
100. Wender R, Brown AM, Fern R, Swanson RA, Farrell K, Ransom BR. Astrocytic glycogen influences axon function and survival during glucose deprivation in central white matter. *J.Neurosci.* 2000;20(18):6804-10.

101. Fujita S, Kawaguchi T. Association of platelet hyper-aggregability with leukoaraiosis. *Acta Neurol.Scand.* 2002;105(6):445-9.
102. Kaplan RD, Solomon GD, Diamond S, Freitag FG. The role of MRI in the evaluation of a migraine population: preliminary data. *Headache* 1987;27(6):315-8.
103. Soges LJ, Cacayorin ED, Petro GR, Ramachandran TS. Migraine: evaluation by MR. *AJNR Am J Neuroradiol.* 1988;9(3):425-9.
104. Ferbert A, Busse D, Thron A. Microinfarction in classic migraine? A study with magnetic resonance imaging findings. *Stroke* 1991;22(8):1010-4.
105. Ziegler DK, Batnitzky S, Barter R, McMillan JH. Magnetic resonance image abnormality in migraine with aura. *Cephalalgia* 1991;11(3):147-50.
106. Fazekas F, Koch M, Schmidt R, Offenbacher H, Payer F, Freidl W et al. The prevalence of cerebral damage varies with migraine type: a MRI study. *Headache* 1992;32(6):287-91.
107. Osborn RE, Alder DC, Mitchell CS. MR imaging of the brain in patients with migraine headaches. *AJNR Am J Neuroradiol.* 1991;12(3):521-4.
108. Cooney BS, Grossman RI, Farber RE, Goin JE, Galetta SL. Frequency of magnetic resonance imaging abnormalities in patients with migraine. *Headache* 1996;36(10):616-21.
109. Gozke E, Ore O, Dortcan N, Unal Z, Cetinkaya M. Cranial magnetic resonance imaging findings in patients with migraine. *Headache* 2004;44(2):166-9.
110. Swartz RH, Kern RZ. Migraine is associated with magnetic resonance imaging white matter abnormalities: a meta-analysis. *Arch.Neurol.* 2004;61(9):1366-8.
111. Dennis M, Warlow C. Migraine aura without headache: transient ischaemic attack or not? *J Neurol Neurosurg Psychiatry* 1992;55(6):437-40.
112. Sacco RL. Risk factors, outcomes, and stroke subtypes for ischemic stroke. *Neurology* 1997;49(5 Suppl 4):S39-S44.
113. Price TR, Psaty B, O'Leary D, Burke G, Gardin J. Assessment of cerebrovascular disease in the Cardiovascular Health Study. *Ann.Epidemiol* 1993;3(5):504-7.
114. Bokura H, Kobayashi S, Yamaguchi S. Distinguishing silent lacunar infarction from enlarged Virchow-Robin spaces: a magnetic resonance imaging and pathological study. *Journal of Neurology* 1998;245(2):116-22.
115. Tatu L, Moulin T, Bogousslavsky J, Duvernoy H. Arterial territories of human brain: brainstem and cerebellum. *Neurology* 1996;47(5):1125-35.
116. Tatu L, Moulin T, Bogousslavsky J, Duvernoy H. Arterial territories of the human brain: cerebral hemispheres. *Neurology* 1998;50(6):1699-708.
117. Scheltens P, Barkhof F, Leys D, Pruvo JP, Nauta JJ, Vermersch P et al. A semiquantitative rating scale for the assessment of signal hyperintensities on magnetic resonance imaging. *J Neurol Sci.* 1993;114(1):7-12.
118. de Leeuw FE, de Groot JC, Achten E, Oudkerk M, Ramos LM, Heijboer R et al. Prevalence of cerebral white matter lesions in elderly people: a population based magnetic resonance imaging study. The Rotterdam Scan Study. *J Neurol.Neurosurg.Psychiatry* 2001;70(1):9-14.
119. Boer JM, Feskens EJ, Schouten EG, Havekes LM, Seidell JC, Kreijboer R et al. Lipid profiles reflecting high and low risk for coronary heart disease: contribution of apolipoprotein E polymorphism and lifestyle. *Atherosclerosis* 1998;136(2):395-402.
120. Alexander JA, Sheppard S, Davis PC, Salverda P. Adult cerebrovascular disease: role of modified rapid fluid-attenuated inversion-recovery sequences. *AJNR Am J Neuroradiol* 1996;17(8):1507-13.
121. Ducros A, Denier C, Joutel A, Cecillon M, Lescoat C, Vahedi K et al. The clinical spectrum of familial hemiplegic migraine associated with mutations in a neuronal calcium channel. *N.Engl.J Med.* 2001;345(1):17-24.
122. Ophoff RA, Terwindt GM, Vergouwe MN, van Eijk R, Oefner PJ, Hoffman et al. Familial hemiplegic migraine and episodic ataxia type-2 are caused by mutations in the Ca²⁺ channel gene CACNL1A4. *Cell* 1996;87(3):543-52.
123. Caplan LR. Migraine and posterior circulation stroke. In: Caplan LR, editor. *Posterior circulation disease: clinical findings, diagnosis and management.* Cambridge, MA: Blackwell Science; 1996. p. 555-6.
124. Bogousslavsky J, Regli F, Maeder P, Meuli R, Nader J. The etiology of posterior circulation infarcts: a prospective study using magnetic resonance imaging and magnetic resonance angiography. *Neurology* 1993;43(8):1528-33.
125. Pessin MS, Lathi ES, Cohen MB, Kwan ES, Hedges TR, III, Caplan LR. Clinical features and mechanism of occipital infarction. *Ann.Neurol.* 1987;21(3):290-9.

126. Caplan LR. Migraine and vertebrobasilar ischemia. *Neurology* 1991;41(1):55-61.
127. Bednarczyk EM, Remler B, Weikart C, Nelson AD, Reed RC. Global cerebral blood flow, blood volume, and oxygen metabolism in patients with migraine headache. *Neurology* 1998;50(6):1736-40.
128. Sanchez del Rio M, Bakker D, Wu O, Agosti R, Mitsikostas DD, Ostergaard L et al. Perfusion weighted imaging during migraine: spontaneous visual aura and headache. *Cephalalgia* 1999;19(8):701-7.
129. Crassard I, Conard J, Bousser MG. Migraine and haemostasis. *Cephalalgia* 2001;21(6):630-6.
130. Tzourio C, El Amrani M, Poirier O, Nicaud V, Bousser MG, Alperovitch A. Association between migraine and endothelin type A receptor (ETA -231 A/G) gene polymorphism. *Neurology* 2001;56(10):1273-7.
131. Dreier JP, Kleeberg J, Petzold G, Priller J, Windmuller O, Orzechowski HD et al. Endothelin-1 potently induces Leao's cortical spreading depression in vivo in the rat: a model for an endothelial trigger of migrainous aura? *Brain* 2002;125(Pt 1):102-12.
132. Goadsby PJ. Pathophysiology of migraine: a disease of the brain. In: Goadsby PJ, Silberstein SD, editors. *Headache*. Boston: Butterworth-Heinemann; 1997. p. 5-25.
133. Eggers AE. New neural theory of migraine. *Med.Hypotheses* 2001;56(3):360-3.
134. Spence JD, Wong DG, Melendez LJ, Nichol PM, Brown JD. Increased prevalence of mitral valve prolapse in patients with migraine. *Can Med Assoc J* 1984;131(12):1457-60.
135. Anzola GP, Magoni M, Guindani M, Rozzini L, Dalla VG. Potential source of cerebral embolism in migraine with aura: a transcranial Doppler study. *Neurology* 1999;52(8):1622-5.
136. Wilmshurst P, Nightingale S. Relationship between migraine and cardiac and pulmonary right-to-left shunts. *Clin.Sci.(Colch.)* 2001;100(2):215-20.
137. Goldberg MP, Ransom BR. New light on white matter. *Stroke* 2003;34(2):330-2.
138. Gallo V, Ghiani CA. Glutamate receptors in glia: new cells, new inputs and new functions. *Trends Pharmacol.Sci.* 2000;21(7):252-8.
139. Featherstone HJ. Clinical features of stroke in migraine: a review. *Headache* 1986;26(3):128-33.
140. Shuaib A, Lee MA. Cerebral infarction in patients with migraine accompaniments. *Headache* 1988;28(9):599-601.
141. Song CJ, Kim JH, Kier EL, Bronen RA. MR imaging and histologic features of subinsular bright spots on T2- weighted MR images: Virchow-Robin spaces of the extreme capsule and insular cortex. *Radiology* 2000;214(3):671-7.
142. Amarenco P. The spectrum of cerebellar infarctions. *Neurology* 1991;41(7):973-9.
143. Amarenco P, Kase CS, Rosengart A, Pessin MS, Bousser MG, Caplan LR. Very small (border zone) cerebellar infarcts. Distribution, causes, mechanisms and clinical features. *Brain* 1993;116 (Pt 1):161-86.
144. Barth A, Bogousslavsky J, Regli F. The clinical and topographic spectrum of cerebellar infarcts: a clinical-magnetic resonance imaging correlation study. *Ann.Neurol.* 1993;33(5):451-6.
145. Canaple S, Bogousslavsky J. Multiple large and small cerebellar infarcts. *J.Neurol.Neurosurg.Psychiatry* 1999;66(6):739-45.
146. Amarenco P, Hauw JJ, Gautier JC. Arterial pathology in cerebellar infarction. *Stroke* 1990;21(9):1299-305.
147. Amarenco P, Levy C, Cohen A, Touboul PJ, Roullet E, Bousser MG. Causes and mechanisms of territorial and nonterritorial cerebellar infarcts in 115 consecutive patients. *Stroke* 1994;25(1):105-12.
148. Caplan LR, Hennerici M. Impaired clearance of emboli (washout) is an important link between hypoperfusion, embolism, and ischemic stroke. *Arch.Neurol.* 1998;55(11):1475-82.
149. Duvernoy H, Delon S, Vannson JL. The vascularization of the human cerebellar cortex. *Brain Res.Bull.* 1983;11(4):419-80.
150. Fessatidis IT, Thomas VL, Shore DF, Hunt RH, Weller RO, Goodland F et al. Assessment of neurological injury due to circulatory arrest during profound hypothermia. An experimental study in vertebrates. *Eur.J.Cardiothorac.Surg.* 1993;7(9):465-72.
151. Olesen J, Friberg L, Olsen TS, Iversen HK, Lassen NA, Andersen AR et al. Timing and topography of cerebral blood flow, aura, and headache during migraine attacks. *Ann Neurol* 1990;28(6):791-8.
152. Friberg L, Olesen J, Lassen NA, Olsen TS, Karle A. Cerebral oxygen extraction, oxygen consumption, and regional cerebral blood flow during the aura phase of migraine. *Stroke* 1994;25(5):974-9.

153. Cutrer FM, Sorensen AG, Weisskoff RM, Ostergaard L, Sanchez dR, Lee EJ et al. Perfusion-weighted imaging defects during spontaneous migrainous aura. *Ann.Neurol.* 1998;43(1):25-31.
154. Couch JR, Hassanein RS. Platelet aggregability in migraine. *Neurology* 1977;27(9):843-8.
155. Silvestrini M, Matteis M, Troisi E, Cupini LM, Zaccari G, Bernardi G. Migrainous stroke and the antiphospholipid antibodies. *Eur.Neurol* 1994;34(6):316-9.
156. D'Andrea G, Cananzi AR, Perini F, Hasselmark L. Platelet models and their possible usefulness in the study of migraine pathogenesis. *Cephalalgia* 1995;15(4):265-71.
157. Cesar JM, Garcia-Avello A, Vecino AM, Sastre JL, Alvarez-Cermeno JC. Increased levels of plasma von Willebrand factor in migraine crisis. *Acta Neurol Scand* 1995;91(5):412-3.
158. Tozzi-Ciancarelli MG, De Matteis G, Di Massimo C, Marini C, Ciancarelli I, Carolei A. Oxidative stress and platelet responsiveness in migraine. *Cephalalgia* 1997;17(5):580-4.
159. Salobir B, Sabovic M, Peternel P, Stegnar M, Grad A. Classic risk factors, hypercoagulability and migraine in young women with cerebral lacunar infarctions. *Acta Neurol.Scand.* 2002;105(3):189-95.
160. Edvinsson L, Goadsby PJ. Neuropeptides in the cerebral circulation: relevance to headache. *Cephalalgia* 1995;15(4):272-6.
161. Hargreaves RJ, Shephard SL. Pathophysiology of migraine--new insights. *Can.J Neurol.Sci.* 1999;26 Suppl 3:S12-S19.
162. Silvestrini M, Baruffaldi R, Bartolini M, Vernieri F, Lanciotti C, Matteis M et al. Basilar and middle cerebral artery reactivity in patients with migraine. *Headache* 2004;44(1):29-34.
163. Sandor PS, Mascia A, Seidel L, De P, V, Schoenen J. Subclinical cerebellar impairment in the common types of migraine: a three-dimensional analysis of reaching movements. *Ann.Neurol.* 2001;49(5):668-72.
164. Harno H, Hirvonen T, Kaunisto MA, Aalto H, Levo H, Isotalo E et al. Subclinical vestibulocerebellar dysfunction in migraine with and without aura. *Neurology* 2003;61(12):1748-52.
165. Terwindt GM, Ophoff RA, van Eijk R, Vergouwe MN, Haan J, Frants RR et al. Involvement of the CACNA1A gene containing region on 19p13 in migraine with and without aura. *Neurology* 2001;56(8):1028-32.
166. Stevanin G, Herman A, Brice A, Durr A. Clinical and MRI findings in spinocerebellar ataxia type 5. *Neurology* 1999;53(6):1355-7.
167. Tournier-Lasserre E. CACNA1A mutations: hemiplegic migraine, episodic ataxia type 2, and the others. *Neurology* 1999;53(1):3-4.
168. Murata Y, Kawakami H, Yamaguchi S, Nishimura M, Kohriyama T, Ishizaki F et al. Characteristic magnetic resonance imaging findings in spinocerebellar ataxia 6. *Arch.Neurol.* 1998;55(10):1348-52.
169. Melberg A, Dahl N, Hetta J, Valind S, Nennesmo I, Lundberg PO et al. Neuroimaging study in autosomal dominant cerebellar ataxia, deafness, and narcolepsy. *Neurology* 1999;53(9):2190-2.
170. Klockgether T, Skalej M, Wedekind D, Luft AR, Welte D, Schulz JB et al. Autosomal dominant cerebellar ataxia type I. MRI-based volumetry of posterior fossa structures and basal ganglia in spinocerebellar ataxia types 1, 2 and 3. *Brain* 1998;121 (Pt 9):1687-93.
171. De Michele G, Mainenti PP, Soricelli A, Di Salle F, Salvatore E, Longobardi MR et al. Cerebral blood flow in spinocerebellar degenerations: a single photon emission tomography study in 28 patients. *J Neurol.* 1998;245(9):603-8.
172. Pullicino P, Ostrow P, Miller L, Snyder W, Munschauer F. Pontine ischemic rarefaction. *Ann.Neurol* 1995;37(4):460-6.
173. Kwa VI, Stam J, Blok LM, Verbeeten B, Jr. T2-weighted hyperintense MRI lesions in the pons in patients with atherosclerosis. Amsterdam Vascular Medicine Group. *Stroke* 1997;28(7):1357-60.
174. Chabriat H, Mrissa R, Levy C, Vahedi K, Taillia H, Iba-Zizen MT et al. Brain stem MRI signal abnormalities in CADASIL. *Stroke* 1999;30(2):457-9.
175. Mantyla R, Pohjasvaara T, Vataja R, Salonen O, Aronen HJ, Standertskjold-Nordenstam CG et al. MRI pontine hyperintensity after supratentorial ischemic stroke relates to poor clinical outcome. *Stroke* 2000;31(3):695-700.
176. Katsarava Z, Schneeweiss S, Kurth T, Kroener U, Fritsche G, Eikermann A et al. Incidence and predictors for chronicity of headache in patients with episodic migraine. *Neurology* 2004;62(5):788-90.
177. Scher AI, Stewart WF, Ricci JA, Lipton RB. Factors associated with the onset and remission of chronic daily headache in a population-based study. *Pain* 2003;106(1-2):81-9.

178. Knight YE, Goadsby PJ. The periaqueductal grey matter modulates trigeminovascular input: a role in migraine? *Neuroscience* 2001;106(4):793-800.
179. Bahra A, Matharu MS, Buchel C, Frackowiak RS, Goadsby PJ. Brainstem activation specific to migraine headache. *Lancet* 2001;357(9261):1016-7.
180. Afridi SK, Matharu MS, Lee L, Kaube H, Friston KJ, Frackowiak RS et al. A PET study exploring the laterality of brainstem activation in migraine using glyceryl trinitrate. *Brain* 2005;128(Pt 4):932-9.
181. Matharu MS, Bartsch T, Ward N, Frackowiak RS, Weiner R, Goadsby PJ. Central neuromodulation in chronic migraine patients with suboccipital stimulators: a PET study. *Brain* 2004;127(Pt 1):220-30.
182. Schenker C, Meier D, Wichmann W, Boesiger P, Valavanis A. Age distribution and iron dependency of the T2 relaxation time in the globus pallidus and putamen. *Neuroradiology* 1993;35(2):119-24.
183. Bartzokis G, Mintz J, Sultzer D, Marx P, Herzberg JS, Phelan CK et al. In vivo MR evaluation of age-related increases in brain iron. *AJNR Am.J.Neuroradiol.* 1994;15(6):1129-38.
184. Rockwell DT, Melhem ER, Bhatia RG. GRASE (gradient- and spin-echo) MR of the brain. *AJNR Am.J.Neuroradiol.* 1997;18(10):1923-8.
185. Thompson KJ, Shoham S, Connor JR. Iron and neurodegenerative disorders. *Brain Res.Bull.* 2001;55(2):155-64.
186. Halliwell B. Role of free radicals in the neurodegenerative diseases: therapeutic implications for antioxidant treatment. *Drugs Aging* 2001;18(9):685-716.
187. Hallgren B, Sourander P. The effect of age on the non-haemin iron in the human brain. *J.Neurochem.* 1958;3(1):41-51.
188. Dobson J. Nanoscale biogenic iron oxides and neurodegenerative disease. *FEBS Lett.* 2001;496(1):1-5.
189. Schenck JF, Zimmerman EA. High-field magnetic resonance imaging of brain iron: birth of a biomarker? *NMR Biomed.* 2004;17(7):433-45.
190. Vymazal J, Brooks RA, Patronas N, Hajek M, Bulte JW, Di Chiro G. Magnetic resonance imaging of brain iron in health and disease. *J.Neurol.Sci.* 1995;134 Suppl:19-26.
191. Iadarola MJ, Berman KF, Zeffiro TA, Byas-Smith MG, Gracely RH, Max MB et al. Neural activation during acute capsaicin-evoked pain and allodynia assessed with PET. *Brain* 1998;121 (Pt 5):931-47.
192. Lipton RB, Pan J. Is migraine a progressive brain disease? *Jama* 2004;291(4):493-4.
193. Lipton RB, Bigal ME. Migraine: epidemiology, impact, and risk factors for progression. *Headache* 2005;45 Suppl 1:S3-S13.
194. Knight YE, Bartsch T, Kaube H, Goadsby PJ. P/Q-type calcium-channel blockade in the periaqueductal gray facilitates trigeminal nociception: a functional genetic link for migraine? *J.Neurosci.* 2002;22(5):RC213.
195. Goadsby PJ. Neurovascular headache and a midbrain vascular malformation: evidence for a role of the brainstem in chronic migraine. *Cephalalgia* 2002;22(2):107-11.
196. Gee JR, Chang J, Dublin AB, Vijayan N. The association of brainstem lesions with migraine-like headache: an imaging study of multiple sclerosis. *Headache* 2005;45(6):670-7.
197. Tortorella P, Rocca MA, Colombo B, Annovazzi P, Comi G, Filippi M. Assessment of MRI abnormalities of the brainstem from patients with migraine and multiple sclerosis. *J.Neurol.Sci.* 2006;244(1-2):137-41.
198. Vymazal J, Hajek M, Patronas N, Giedd JN, Bulte JW, Baumgarner C et al. The quantitative relation between T1-weighted and T2-weighted MRI of normal gray matter and iron concentration. *J.Magn Reson.Imaging* 1995;5(5):554-60.
199. Aoki S, Okada Y, Nishimura K, Barkovich AJ, Kjos BO, Brasch RC et al. Normal deposition of brain iron in childhood and adolescence: MR imaging at 1.5 T. *Radiology* 1989;172(2):381-5.
200. Pujol J, Junque C, Vendrell P, Grau JM, Marti-Vilalta JL, Olive C et al. Biological significance of iron-related magnetic resonance imaging changes in the brain. *Arch.Neurol.* 1992;49(7):711-7.
201. Kruit MC, Launer LJ, Ferrari MD, van Buchem MA. Brain stem and cerebellar hyperintense lesions in migraine. *Stroke* 2006;37(4):1109-12.
202. Kruit MC, Launer LJ, Ferrari MD, van Buchem MA. Infarcts in the posterior circulation territory in migraine. The population-based MRI CAMERA study. *Brain* 2005;128(Pt 9):2068-77.

203. Brignole M, Alboni P, Benditt DG, Bergfeldt L, Blanc JJ, Bloch Thomsen PE et al. Guidelines on management (diagnosis and treatment) of syncope--update 2004. *Europace*. 2004;6(6):467-537.
204. Markush RE, Karp HR, Heyman A, O'Fallon WM. Epidemiologic study of migraine symptoms in young women. *Neurology* 1975;25(5):430-5.
205. Selby G, LANCE JW. Observations on 500 cases of migraine and allied vascular headache. *J.Neurol.Neurosurg.Psychiatry* 1960;23:23-32.
206. Shechter A, Stewart WF, Silberstein SD, Lipton RB. Migraine and autonomic nervous system function: a population-based, case-control study. *Neurology* 2002;58(3):422-7.
207. Havanka-Kanniainen H, Tolonen U, Myllyla VV. Autonomic dysfunction in adult migraineurs. *Headache* 1986;26(8):425-30.
208. Havanka-Kanniainen H, Tolonen U, Myllyla VV. Autonomic dysfunction in migraine: a survey of 188 patients. *Headache* 1988;28(7):465-70.
209. Havanka-Kanniainen H. Cardiovascular reflex responses during migraine attack. *Headache* 1986;26(9):442-6.
210. Pogacnik T, Sega S, Pecnik B, Kiauta T. Autonomic function testing in patients with migraine. *Headache* 1993;33(10):545-50.
211. Boiardi A, Munari L, Milanese I, Paggetta C, Lamperti E, Bussone G. Impaired cardiovascular reflexes in cluster headache and migraine patients: evidence for an autonomic dysfunction. *Headache* 1988;28(6):417-22.
212. Mikamo K, Takeshima T, Takahashi K. Cardiovascular sympathetic hypofunction in muscle contraction headache and migraine. *Headache* 1989;29(2):86-9.
213. Gotoh F, Komatsumoto S, Araki N, Gomi S. Noradrenergic nervous activity in migraine. *Arch.Neurol.* 1984;41(9):951-5.
214. Yakinci C, Mungen B, Er H, Durmaz Y, Karabiber H. Autonomic nervous system function in childhood migraine. *Pediatr.Int.* 1999;41(5):529-33.
215. Kanjwal Y, Kosinski D, Grubb BP. The postural orthostatic tachycardia syndrome: definitions, diagnosis, and management. *Pacing Clin.Electrophysiol.* 2003;26(8):1747-57.
216. Chen L, Chen MH, Larson MG, Evans J, Benjamin EJ, Levy D. Risk factors for syncope in a community-based sample (the Framingham Heart Study). *Am.J.Cardiol.* 2000;85(10):1189-93.
217. Kaufmann H. Consensus statement on the definition of orthostatic hypotension, pure autonomic failure and multiple system atrophy. *Clin.Auton.Res.* 1996;6(2):125-6.
218. Low PA, Opfer-Gehrking TL, Textor SC, Benarroch EE, Shen WK, Schondorf R et al. Postural tachycardia syndrome (POTS). *Neurology* 1995;45(4 Suppl 5):S19-S25.
219. Ganzeboom KS, Colman N, Reitsma JB, Shen WK, Wieling W. Prevalence and triggers of syncope in medical students. *Am.J.Cardiol.* 2003;91(8):1006-8, A8.
220. Colman N, Nahm K, Ganzeboom KS, Shen WK, Reitsma J, Linzer M et al. Epidemiology of reflex syncope. *Clin.Auton.Res.* 2004;14 Suppl 1:9-17.
221. Savage DD, Corwin L, McGee DL, Kannel WB, Wolf PA. Epidemiologic features of isolated syncope: the Framingham Study. *Stroke* 1985;16(4):626-9.
222. Thijs RD, Wieling W, Kaufmann H, van DG. Defining and classifying syncope. *Clin.Auton.Res.* 2004;14 Suppl 1:4-8.
223. Peroutka SJ. Migraine: a chronic sympathetic nervous system disorder. *Headache* 2004;44(1):53-64.
224. Thijs RD, Kruit MC, van Buchem MA, Ferrari MD, Launer LJ, van Dijk JG. Syncope in migraine: the population-based CAMERA study. *Neurology* 2006;66(7):1034-7.
225. Consensus statement on the definition of orthostatic hypotension, pure autonomic failure, and multiple system atrophy. The Consensus Committee of the American Autonomic Society and the American Academy of Neurology. *Neurology* 1996;46(5):1470.
226. Kenny RA, Shaw FE, O'Brien JT, Scheltens PH, Kalaria R, Ballard C. Carotid sinus syndrome is common in dementia with Lewy bodies and correlates with deep white matter lesions. *J.Neurol.Neurosurg.Psychiatry* 2004;75(7):966-71.
227. Dobkin BH. Orthostatic hypotension as a risk factor for symptomatic occlusive cerebrovascular disease. *Neurology* 1989;39(1):30-4.
228. Eigenbrodt ML, Rose KM, Couper DJ, Arnett DK, Smith R, Jones D. Orthostatic hypotension as a risk factor for stroke: the atherosclerosis risk in communities (ARIC) study, 1987-1996. *Stroke* 2000;31(10):2307-13.

229. Fernando MS, Simpson JE, Matthews F, Brayne C, Lewis CE, Barber R et al. White matter lesions in an unselected cohort of the elderly: molecular pathology suggests origin from chronic hypoperfusion injury. *Stroke* 2006;37(6):1391-8.
230. Pantoni L, Garcia JH. Pathogenesis of leukoaraiosis: a review. [Review] [114 refs]. *Stroke* 1997;28(3):652-9.
231. Kario K, Hoshida S, Shimada K. Extreme-dipper, abnormal diurnal blood pressure variation in the elderly hypertensive, and orthostatic hypertension. *J.Hum.Hypertens.* 1998;12(2):141-2.
232. Bakker SL, de Leeuw FE, de Groot JC, Hofman A, Koudstaal PJ, Breteler et al. Cerebral vasomotor reactivity and cerebral white matter lesions in the elderly. *Neurology* 1999;52(3):578-83.
233. de Leeuw FE, de Groot JC, Oudkerk M, Witteman JC, Hofman A, Van GJ et al. A follow-up study of blood pressure and cerebral white matter lesions. *Ann.Neurol.* 1999;46(6):827-33.
234. Eguchi K, Kario K, Hoshida S, Hoshida Y, Ishikawa J, Morinari M et al. Greater change of orthostatic blood pressure is related to silent cerebral infarct and cardiac overload in hypertensive subjects. *Hypertens.Res.* 2004;27(4):235-41.
235. Tietjen GE. Stroke and migraine linked by silent lesions. *Lancet Neurol.* 2004;3(5):267.
236. Kruit MC, Launer LJ, van Buchem MA, Terwindt GM, Ferrari MD. MRI findings in migraine. *Rev.Neurol.(Paris)* 2005;161(6-7):661-5.
237. Iizuka T, Sakai F, Yamakawa K, Suzuki K, Suzuki N. Vasogenic leakage and the mechanism of migraine with prolonged aura in Sturge-Weber syndrome. *Cephalalgia* 2004;24(9):767-70.
238. Ghabriel MN, Lu MX, Leigh C, Cheung WC, Allt G. Substance P-induced enhanced permeability of dura mater microvessels is accompanied by pronounced ultrastructural changes, but is not dependent on the density of endothelial cell anionic sites. *Acta Neuropathol.(Berl)* 1999;97(3):297-305.
239. Dohmen C, Sakowitz OW, Fabricius M, Bosche B, Reithmeier T, Ernestus RI et al. Spreading depolarizations occur in human ischemic stroke with high incidence. *Ann.Neurol.* 2008;63(6):720-8.
240. DaSilva AF, Granziera C, Snyder J, Hadjikhani N. Thickening in the somatosensory cortex of patients with migraine. *Neurology* 2007;69(21):1990-5.
241. DaSilva AF, Granziera C, Tuch DS, Snyder J, Vincent M, Hadjikhani N. Interictal alterations of the trigeminal somatosensory pathway and periaqueductal gray matter in migraine. *Neuroreport* 2007;18(4):301-5.
242. Welch KM. Iron in the migraine brain; a resilient hypothesis. *Cephalalgia* 2008.
243. Kurth T, Gaziano JM, Cook NR, Logroscino G, Diener HC, Buring JE. Migraine and risk of cardiovascular disease in women. *Jama* 2006;296(3):283-91.
244. Rocca MA, Colombo B, Pagani E, Falini A, Codella M, Scotti G et al. Evidence for cortical functional changes in patients with migraine and white matter abnormalities on conventional and diffusion tensor magnetic resonance imaging. *Stroke* 2003;34(3):665-70.
245. Ardila A, Sanchez E. Neuropsychologic symptoms in the migraine syndrome. *Cephalalgia* 1988;8(2):67-70.
246. Farmer K, Cady R, Bleiberg J, Reeves D. A pilot study to measure cognitive efficiency during migraine. *Headache* 2000;40(8):657-61.
247. Hooker WD, Raskin NH. Neuropsychologic alterations in classic and common migraine. *Arch.Neurol.* 1986;43(7):709-12.
248. Le Pira F, Zappala G, Giuffrida S, Lo Bartolo ML, Reggio E, Morana R et al. Memory disturbances in migraine with and without aura: a strategy problem? *Cephalalgia* 2000;20(5):475-8.
249. Mulder EJ, Linssen WH, Passchier J, Orlebeke JF, de Geus EJ. Interictal and postictal cognitive changes in migraine. *Cephalalgia* 1999;19(6):557-65.
250. Bell BD, Primeau M, Sweet JJ, Lofland KR. Neuropsychological functioning in migraine headache, nonheadache chronic pain, and mild traumatic brain injury patients. *Arch.Clin.Neuropsychol.* 1999;14(4):389-99.
251. Gaist D, Pedersen L, Madsen C, Tsiropoulos I, Bak S, Sindrup S et al. Long-term effects of migraine on cognitive function: a population-based study of Danish twins. *Neurology* 2005;64(4):600-7.
252. Jelicic M, van Boxtel MP, Houx PJ, Jolles J. Does migraine headache affect cognitive function in the elderly? Report from the Maastricht Aging Study (MAAS). *Headache* 2000;40(9):715-9.
253. Pearson AJ, Chronicle EP, Maylor EA, Bruce LA. Cognitive function is not impaired in people with a long history of migraine: a blinded study. *Cephalalgia* 2006;26(1):74-80.

254. Ishizaki K, Mori N, Takeshima T, Fukuhara Y, Ijiri T, Kusumi M et al. Static stabilometry in patients with migraine and tension-type headache during a headache-free period. *Psychiatry Clin.Neurosci.* 2002;56(1):85-90.
255. Terwindt GM, Ophoff RA, Haan J, Vergouwe MN, van Eijk R, Frants RR et al. Variable clinical expression of mutations in the P/Q-type calcium channel gene in familial hemiplegic migraine. Dutch Migraine Genetics Research Group. *Neurology* 1998;50(4):1105-10.
256. Dichgans M, Herzog J, Freilinger T, Wilke M, Auer DP. 1H-MRS alterations in the cerebellum of patients with familial hemiplegic migraine type 1. *Neurology* 2005;64(4):608-13.
257. Felmeden DC, Blann AD, Spencer CG, Beevers DG, Lip GY. A comparison of flow-mediated dilatation and von Willebrand factor as markers of endothelial cell function in health and in hypertension: relationship to cardiovascular risk and effects of treatment: a substudy of the Anglo-Scandinavian Cardiac Outcomes Trial. *Blood Coagul.Fibrinolysis* 2003;14(5):425-31.
258. Conlan MG, Folsom AR, Finch A, Davis CE, Sorlie P, Marcucci G et al. Associations of factor VIII and von Willebrand factor with age, race, sex, and risk factors for atherosclerosis. The Atherosclerosis Risk in Communities (ARIC) Study. *Thromb.Haemost.* 1993;70(3):380-5.
259. Thorand B, Baumert J, Doring A, Schneider A, Chambless L, Lowel H et al. Association of cardiovascular risk factors with markers of endothelial dysfunction in middle-aged men and women. Results from the MONICA/KORA Augsburg Study. *Thromb.Haemost.* 2006;95(1):134-41.
260. Tietjen GE. Migraine and ischaemic heart disease and stroke: potential mechanisms and treatment implications. *Cephalalgia* 2007;27(8):981-7.
261. Kowa H, Fusayasu E, Ijiri T, Ishizaki K, Yasui K, Nakaso K et al. Association of the insertion/deletion polymorphism of the angiotensin I-converting enzyme gene in patients of migraine with aura. *Neurosci.Lett.* 2005;374(2):129-31.
262. Paterna S, Di Pasquale P, D'Angelo A, Seidita G, Tuttolomondo A, Cardinale A et al. Angiotensin-converting enzyme gene deletion polymorphism determines an increase in frequency of migraine attacks in patients suffering from migraine without aura. *Eur.Neurol.* 2000;43(3):133-6.
263. Kowa H, Yasui K, Takeshima T, Urakami K, Sakai F, Nakashima K. The homozygous C677T mutation in the methylenetetrahydrofolate reductase gene is a genetic risk factor for migraine. *Am.J Med.Genet.* 2000;96(6):762-4.
264. Scher AI, Terwindt GM, Verschuren WM, Kruit MC, Blom HJ, Kowa H et al. Migraine and MTHFR C677T genotype in a population-based sample. *Ann.Neurol.* 2006;59(2):372-5.
265. Lea RA, Ovcaric M, Sundholm J, Solyom L, MacMillan J, Griffiths LR. Genetic variants of angiotensin converting enzyme and methylenetetrahydrofolate reductase may act in combination to increase migraine susceptibility. *Brain Res.Mol.Brain Res.* 2005;136(1-2):112-7.
266. Borroni B, Rao R, Liberini P, Venturelli E, Cossandi M, Archetti S et al. Endothelial nitric oxide synthase (Glu298Asp) polymorphism is an independent risk factor for migraine with aura. *Headache* 2006;46(10):1575-9.

LIST OF PUBLICATIONS

- Lamb HJ, Doornbos J, van der Velde EA, Kruit MC, Reiber JH, de Roos A. Echo planar MRI of the heart on a standard system: validation of measurements of left ventricular function and mass. *J. Comput. Assist. Tomogr.* 1996;942-9.
- Bode PJ, Edwards MJ, Kruit MC, van Vugt AB. Sonography in a clinical algorithm for early evaluation of 1671 patients with blunt abdominal trauma. *AJR* 1999;905-11.
- Edwards MJ, Frankema SP, Kruit MC, Bode PJ, Breslau PJ, van Vugt AB. Efficiency of a standardized diagnostic protocol in trauma management. *Eur. J. Ultrasound* 2001;81-6.
- Edwards MJ, Frankema SP, Kruit MC, Bode PJ, Breslau PJ, van Vugt AB. Routine cervical spine radiography for trauma victims: Does everybody need it? *J. Trauma* 2001;529-34.
- Kruit MC, van Buchem MA, Hofman PA, Bakkers JT, Terwindt GM, Ferrari MD, Launer LJ. Migraine as a risk factor for subclinical brain lesions. *JAMA* 2004;427-34.
- Kruit MC, Launer LJ, Ferrari MD, van Buchem MA. Infarcts in the posterior circulation territory in migraine. The population-based MRI CAMERA study. *Brain* 2005;2068-77.
- Kruit MC, Launer LJ, van Buchem MA, Terwindt GM, Ferrari MD. Migraine as a Risk Factor for White Matter Lesions, Silent Infarctions, and Ischemic Stroke: The Evidence for a Link. *Headache Currents* 2005;62-70.
- Kruit MC, Launer LJ, van Buchem MA, Terwindt GM, Ferrari MD. MRI findings in migraine. *Rev. Neurol. (Paris)* 2005;661-5.
- Kruit MC, Launer LJ, Ferrari MD, van Buchem MA. Brain stem and cerebellar hyperintense lesions in migraine. *Stroke* 2006;1109-12.
- Scher AI, Terwindt GM, Verschuren WM, Kruit MC, Blom HJ, Kowa H, Frants RR, van den Maagdenberg AM, van Buchem M, Ferrari MD, Launer LJ. Migraine and MTHFR C677T genotype in a population-based sample. *Ann. Neurol.* 2006;372-5.
- Thijs RD¹, Kruit MC¹, van Buchem MA, Ferrari MD, Launer LJ, van Dijk JG. Syncope in migraine: the population-based CAMERA study. *Neurology* 2006;1034-7.
- Schmitz N, Admiraal-Behloul F, Arkink EB, Kruit MC, Schoonman GG, Ferrari MD, van Buchem MA. Attack-frequency and disease-duration as indicators for brain damage in migraine. *Headache* 2008; 48: 1044-1065.
- Schmitz N, Arkink EB, Mulder M, Rubia K, Admiraal-Behloul F, Schoonman GG, Kruit MC, Ferrari MD, van Buchem MA. Frontal lobe structure and executive function in migraine patients. *Neuroscience Letters* 2008; 92–96.
- Kruit MC, Launer LJ, Overbosch J, van Buchem MA, Ferrari MD. Iron accumulation in deep brain nuclei in migraine. A population-based Magnetic Resonance Imaging study. *Cephalalgia* 2008; 29: 351–359.
- Wilbrink LA, Ferrari MD, Kruit MC, Haan J. Neuroimaging in trigeminal autonomic cephalgias: when, how, and of what? *Curr. Opin. Neurol.* 2009; 22: 247-253.
- Kruit MC, van Buchem MA, Launer LJ, Terwindt GM, Ferrari MD. Migraine is associated with an increased risk of white matter lesions, subclinical infarcts and brain iron accumulation. The population-based MRI CAMERA-study. *Cephalalgia* 2009, June 9.

CURRICULUM VITAE

Mark Christian Kruit was born on 7 October 1972 in Enschede, the Netherlands. In 1991 he graduated from the Ichthus College in Enschede (Gymnasium B), and started to study medicine at Leiden University. In 1996 he obtained his masters degree in medicine, in 1998 his medical degree. As a student he became involved in a research project into the efficiency of analyzing cardiac MR-images at the LUMC department of Radiology (dr. H.J. Lamb and prof.dr. A. de Roos), and during a scientific internship he evaluated the role of abdominal ultrasound in blunt abdominal trauma at the same department (drs. P.J. Bode). In 1998 he started with the PhD research project described in this thesis under the supervision of prof.dr. M.A. van Buchem (department of Radiology), prof.dr. M.D. Ferrari (department of Neurology) and dr. L.J. Launer (then at RIVM, currently at NIA, NIH), and funded by a grant from the Netherlands Heart Association. In July 2002 he started his residency program in Radiology at the LUMC (prof.dr. J.L. Bloem). In July 2007 he was registered as a radiologist, and from 2006 to 2008 he worked as a clinical fellow in Neuroradiology (drs. B.M. Verbist). Hereafter he continued to work in de LUMC department of Radiology as Neuroradiologist.

The work described in this thesis was presented in national and international Radiological and Neurological scientific meetings, and received a number of awards, including the “Pramod R. Saxena Prize” (2005, Dutch Headache Society), and was summarized during the European Headache and Migraine Trust International Congress in an invited review lecture (September 2008). From 2007 the author is as principal investigator involved in the multicenter population-based CAMERA II-study: “Brain damage in migraine: progression, relevance and etiology.” for which grants were received from the Netherlands Heart Association and from the National Institute of Neurological Disorders and Stroke (R01). In the LUMC department of Radiology he is responsible for all research activities related to “Neuroradiology of primary headaches”.

Mark lives in Oegstgeest with his wife Elise, and his daughters Julia and Rozemarijn.