Familial Hemiplegic Migraine, A Case Report Of Attack Associated Findings

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Citation

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Abstract

Recent studies have shed more light onto the genetical basis of familial hemiplegic migraine (FHM) as a channelopathy due to 3 abnormal loci of the brain specific P/Q type calcium channel alpha 1A subunit gene (CACNA1A) on chromosome 1 and 19p13 [1]. CACNA1A regulates the release of various neurotransmitters, probably including serotonin. Circulatory changes detected by different imaging techniques during migraine also support the pathophysiological role of spreading depression at least in migraine with aura [2]. Nevertheless there is much left to learn about the specific pathophysiology leading to clinically recognized phenomena such as headache and transient palsy. In this report we present some neurophysiological and imaging data from a 32-year old man with FHM, which were recorded during a hemiplegic attack lasting for 7 days.

INTRODUCTION

Recent studies have shed more light onto the genetical basis of familial hemiplegic migraine (FHM) as a channelopathy due to 3 abnormal loci of the brain specific P/Q type calcium channel alpha 1A subunit gene (CACNA1A) on chromosome 1 and 19p13 [$_1$]. CACNA1A regulates the release of various neurotransmitters, probably including serotonin. Circulatory changes detected by different imaging techniques during migraine also support the pathophysiological role of spreading depression at least in migraine with aura [$_2$]. Nevertheless there is much left to learn about the specific pathophysiology leading to clinically recognized phenomena such as headache and transient palsy. In this report we present some neurophysiological and imaging data from a 32-year old man with FHM, which were recorded during a hemiplegic attack lasting for 7 days.

CASE REPORT

A young Sudanese man with positive maternal history in respect of FHM developed strict left-sided throbbing headache with initial blurred vision and somnolence to transient coma followed by plegia of the right arm recurring at variable intervals. On neurological examination deep tendon reflexes were brisk and plantar responses were flexor on both sides. There was a partial pinprick and proprioception sensory loss on his right side but no ataxia or vegetative impairment. MRI (T2- and T1-weighted sequences with Gadolinium) 7 hours after onset of symptoms revealed no infarction or localized edema. On the surface-EEG, transient slowing of alpha background activity with delta-waves in the left precentral region and intermittent frontotemporal slowing (continuous theta-dysrhythmia) on both sides were seen. Transcranial magnetically evoked motor potentials (MEP) showed hyperexcitability of the left motor cortex (Table 1), which is thought to be due to facilitated cortical interneurons leading to a significant higher amplitude of the right abductor digiti quinti compound muscle potential.

Figure 1

Table 1: Motor evoked potentials (MEP)

abductor digiti quinti muscle		right*	left
cortical stimulation	latency [ms]	23,0	23,8
	amplitude [mV]	2,8	0,9
spinal stimumation	latency [ms]	16,0	14,8
	amplitude [mV]	9,1	10,0
CMCT		7,0	9,0
tibialis anterior muscle			
cortical stimulation	latency [ms]	30,4	30,0
	amplitude [mV]	0,37	0,42

* clinically affected side

Legend:

CMCT: central motor conduction time

Tc-99m HMPAO-SPECT 3 days after onset of symptoms disclosed hyperperfusion in the left thalamus region (Fig. 1). Angle corrected peak systolic (PSV) and enddiastolic velocity (EDV) detected by TCCD (Table 2) was elevated in both MCA and other basal arteries while pulsatility was reduced owing to a diffuse dilatation of brain arterioles.

Figure 2

Figure 1: Tc-99m HMPAO-SPECT: Hyperperfusion in the left thalamus region

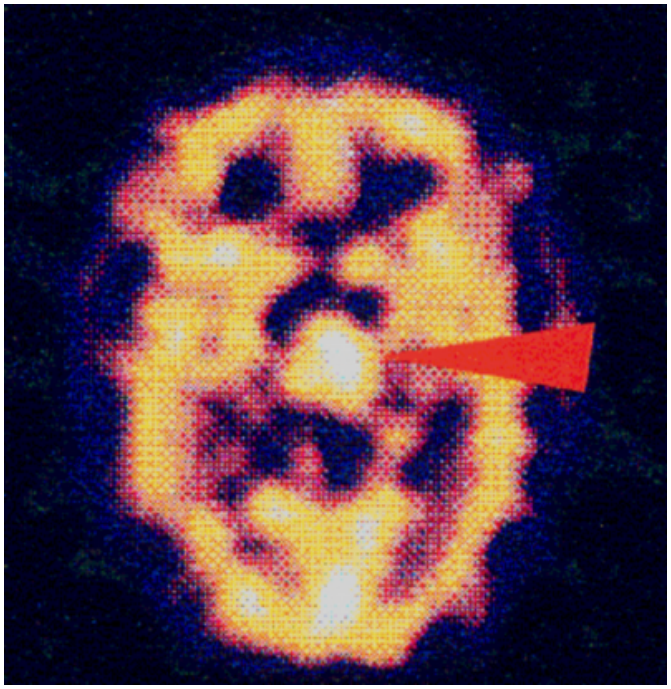

Figure 3

Table 2: TCCD findings

	right side			left side		
	PSV [m/s] SD	EDV [m/s]	RI SD	PSV [m/s] SD	EDV [m/s]	RI SD
MCA	1,29 1,3	0,68	0,47 -1,25	1,36 1,65	0,68	0,5 -0,9
ACA	0,6 -1,16	0,18	0,69 1,6	0,8 0,26	0,42	0,47 -1,3
PCA	0,76 0,9	0,41	0,46 -2,2	0,74 0,78	0,34	0,54 -0,6

reference values are taken from unpublished own data of an age matched healthy population

Legend:

PSV: peak systolic velocity

EDV: enddiastolic velocity

RI: Resistance index

SD: standard deviation

DISCUSSION

Migraine is considered to be a functional neurological disorder, in which changes of vessel diameter seem to play a significant role, at least as an epiphenomenon of a different primary cause, such as a midbrain “migraine-generator” induced release of multiple proinflammatoric and excitatoric mediators (including substance P, CGRP, NO, neuropeptide Y, neurokinin A, VIP) [2, 3]. Conflicting data exist for BFV as an indirect marker for vessel diameter as well as for MEP as a method proven to show state of cortex excitability in different types and states of migraine [4,5,6]. In respect of FHM increased interictal cortical excitability, complicated by decreased excitability of the affected side was found in 10 patients [7]. SPECT studies with Tc-99m HMPAO revealed asymmetric perfusion in the upper frontal and occipital parts of the brain in patients with migraine leading to the hypothesis that impaired regional cerebral vascular autoregulation may exist even during headache-free intervals [8]. Decreased cerebral perfusion, as indicated by brain SPECT, is considered to reflect aura rather than migraine headache [12]. In FHM, hyperperfusion was detected during attack on SPECT [13] and MRI [9].

In this patient with recurrent strict unilateral headache and long lasting contralateral weakness TCCD revealed abnormalities in BFV during attack, which are consistent with dilatation of cerebral arterioles on both, clinical affected and unaffected hemispheres. Intermittent subcortical theta-dysrhythmia was seen in EEG on both sides and over the left precental region. Moreover, our findings suggest a “migraine generator”, which may be responsible for headache and hyperexcitability of left motor cortex. Cerebrovascular resistance is regulated by cerebellar and brainstem structures, such as fastigial nucleus, which seem to activate the NO pathways leading to vessel dilatation and hyperperfusion [14]. Our SPECT findings with hyperperfusion in the left thalamus support this hypothesis. Motor pathway itself shows normal central motor conduction time on both sides. With magnetical cortex stimulation I-waves are generated via interneurons to Betz-giant-cells [10, 11] in contrast to electrical cortex stimulation, where D-waves are generated by stimulating the axons of Betz-giant-cells. It is well known that imagination of muscle movement can facilitate amplitudes in magnetically evoked muscle responses, probably by using the neuronal pathway between limbic system, striatum, thalamus and motor-cortex interneurons [10]. In this case of FHM we believe that motor cortex activation due to a “migraine generator” leads by thalamocortical pathways to hyperexcitability and continuous depolarization of motor neurons. Consequently, motor disturbances, localized brain edema and even infarction during attacks may be found [9]. Further systematical studies are needed to varify this hypothesis.

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