Changes of Blood Oxygenation in a Rat Migraine Model

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Introduction

The mechanism of action during migraine includes increased neuronal activity. Increased brain activity and changes in sodium fluxes during migraine can initiate an increased energy demand and changes in brain oxygen consumption. In our studies we used nitroglycerin to initiate migraine. The biological effect of nitroglycerin was noticed many years ago during production of dynamite. More recently, it was discovered that the active component of nitroglycerin is NO, which is produced from nitroglycerin by mitochondrial aldehyde dehydrogenase.

Experimental

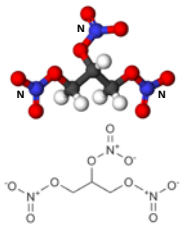
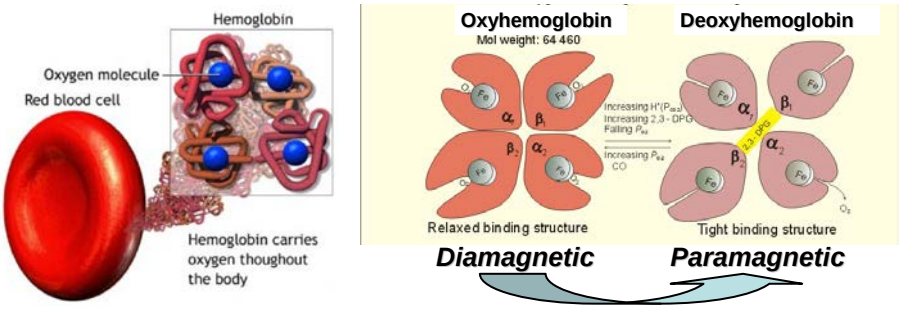


Figure 1. Molecular structure of nitroglycerin.

In the current experiments minor changes in blood oxygenation were detected with increased sensitivity at 21.1T by changes in magnetic field values in brain initiated by changes in magnetic susceptibility as a result of changes in hemoglobin oxygen content. Experiments were performed using nitroglycerin (**Figure 1**) in rat migraine model (1). Proton and sodium FID detection was performed each minute allowing observation at onset of migraine and its time course.

Results and Discussion

High neuronal activity initiates changes in brain oxygenation. Hemoglobin in red blood cells performs transport of oxygen throughout our body. Decrease of oxygen profoundly changes the structure of hemoglobin. Without oxygen, iron in hemoglobin creates large changes in magnetic susceptibility and the relaxation time of surrounding water, which is called the BOLD effect blood oxygenation level).



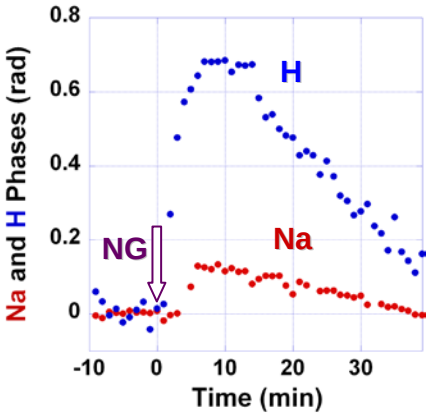


Figure 2. Time course of the proton and sodium MR signal phases in rat brain during migraine.

The time course of the nitroglycerin effect is represented by changes in phase of proton and sodium MR signals from rat brain (**Figure 2**). At time zero, nitroglycerin was injected into the peritoneal cavity. Increased brain activation is producing large deoxygenation and consequently a large change in magnetic susceptibility throughout brain. These changes are detected by an increase in phase shift of the brain MR signals for both sodium and proton. Later on, MR phases are slowly coming back representing a vasodilatation of blood vessels (2) and increase in oxygen supply. It is important to note that the difference in phase shifts between proton and sodium is ~ 4 times, which is corresponding to the ~ 4 times difference in their gyro-magnetic ratio. This result validates that the observed phase changes are due to the altered magnetic field triggered by alterations in magnetic susceptibility throughout the rat brain during migraine.

Conclusions

BOLD effect is a vital part of the nitroglycerin-triggered migraine mechanism which will be further investigated together with sodium MRI.

Acknowledgements

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References

[1] Harrington, M.G., *et al.,* Cephalalgia, **12,** 1254-65 (2011).
[2] Greco, *et al.,* Cephalalgia, **31(2),** 190-8 (2011).