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Time-of-day modulations of rCBF response in functional brain imaging studies: a meta-analysis

Christina Schmidt[1,7], Thanh Dang-Vu[1,3], Pierre Orban[1], Gilles Vandewalle[1], Arnaud Destrebecqz[5], Arnaud D'Argembeau[1,4], Gaëtan Garraux[1,3], Steven Laureys[1,3], Françoise Lekeu[1,2], Steve Majerus[4], Eric Salmon[1,3], Fabien Perrin[6], Derk-Jan Dijk[8], Pierre Maquet[1,3], Fabienne Collette[1,2], Philippe Peigneux[1-3]

[1]Cyclotron Research Centre, Liege University, Belgium, [2]Neuropsychology Unit, Cognitive Science Department, Liege University, Belgium, [3]Neurology Department, CHU Liege, Belgium, [4]Cognitive Psychopathology Unit, Cognitive Science Department, Liege University, Belgium, [5]LEAD, University of Bourgogne, France, [6]CNRS Research Unit 5020, University Claude Bernard, Lyon, France, [7]Center for Chronobiology, Psychiatric University Clinic, Basel, Switzerland, [8]Surrey Sleep Research Centre, University of Surrey, UK

Objective: Circadian variations (time of day) and homeostatic sleep pressure (elapsed awake time) determine our sleep-wake cycle [1] and affect several neurophysiological parameters (e.g., central temperature and melatonine release), as well as the level of performance in a series of cognitive functions [2]. In the context of functional brain imaging studies, we aimed to evidence the set of brain areas in which rCBF is modulated by the moment of scan acquisition.

Methods: From 22 rCBF PET studies previously conducted in the Cyclotron Research Centre, 309 subjects were included in this meta-analysis. All PET data were acquired between 9:00 and 18:00 on a Siemens CTI 951 R 16/31 scanner in 3D mode using the H215O technique. The resulting 3736 scans were obtained in motor, visual, auditory, tactile and somatosensory modalities from a wide range of experimental conditions that included among others executive functions, procedural learning, semantic, episodic and emotional memories, pain perception, praxis and phonological processing, and resting state. Data were analysed in SPM2 (http://www.fil.ion.ucl.ac.uk/spm/spm2) using the general linear model. Covariate of interest was the clock time of each scan acquisition, reported on the average adjusted curve of the circadian component of body temperature rhythm (nadir 6:00, peak 20:00-22:00). Reported results are significant at pcorr < .05 after correction in the whole brain volume.

Results & Discussion: Regional CBF is positively correlated with time of day in a large set of brain areas. Those areas in which activity increased along the day were thalamus and hypothalamus including the suprachiasmatic region (8 0 –10 mm as identified in [3]; Z = 4.99; cross hair on Figure), limbic regions including the amygdala, hippocampus, parahippocampal and cingulate gyri, the cerebellum (culmen), pre- and post-central areas, precuneus, middle, medial and superior frontal gyri, and superior temporal gyrus.

It should be noticed that the homeostatic component was not fully controlled in this post-hoc analysis. Indeed, different subjects scanned at the same time of day may have been awake for a different amount of time, meaning a different sleep pressure. Such control should be taken into account in further studies, considering that our sleep-wake cycle is determined by the interaction

between circadian and homeostatic processes [1]. Also, it is worth mentioning that this study was not aimed to identify rCBF variations specifically related to particular aspects of cognition or sensory modalities, since the analysis was conducted on PET scans obtained in a wide variety of conditions. Rather, by gathering many different conditions in a single analysis, our results highlight the set of brain areas in which circadian and homeostatic influences might be expressed.

Conclusions: Our meta-analysis suggest that time of day exerts its influence on rCBF distribution in a large set of brain areas in the context of functional brain imaging studies. Respective contributions of circadian and homeostatic components still remain to be delineated in further, dedicated, experiments.

References & Acknowledgements: [1] Achermann & Borbely (2003) *Front Biosci*, 8:683-693
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