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How Circadian Rhythms do Affect Anesthesiology and Research

Editorial

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Two Billion Years ago the earth encountered two major changes: Sunlight and oxygen. Therefore, all organisms developed mechanisms to sense oxygen or light [1, 2]. While sensing oxygen seems very important for health and well-being, the sensing of light and its impact on health is not well understood yet. In fact, oxygen probes help physicians and anesthesiologists to monitor the oxygen content in our patient's blood. If those levels are low we would immediately treat those conditions. However, light seems less appreciated even though both systems share many similarities – at least on a molecular level.

For oxygen we have a transcription factor named 'hypoxia inducible factor 1' which is a well-known adaptive mechanisms to correct conditions of low oxygen availability [3]. E.g. if oxygen levels drop and HIF1 becomes active genes such as VEGF are activated and help the body to build up new vessels to improve tissue perfusion and thereby oxygen levels [4].

For light we have the circadian rhythm proteins as light and in particular the switch between light and darkness has led to the development of a circadian system in all living organisms [2]. The key proteins of the circadian system are named Clock, Cryptochrome or Period and belong to the same protein family as HIF1A. It is a so-called superfamily of PAS domain positive proteins [2]. In fact, the PAS domain has been shown to sense light or oxygen [5].

However, while both systems seem equally important from an evolutionary stand point, it is not clinical practice yet to monitor light. Interestingly, there is rising evidence for a high impact of light and the light dependent circadian rhythms for health and disease. E.g. disrupted circadian rhythms are associated with metabolic disorders [6-9]. Light at night can increase triglyceride levels and increase body fat [10]. Sleep deprivation leads to insulin resistance and diabetes [6]. In fact many diseases show a circadian pattern [1, 2, 11]. As such, the occurrence of heart attacks or strokes are linked to certain time points during the day [11].

Everyday medication have different effects during a 24 h time period [12]. The one hundred top selling drugs have circadian targets and therefore blood pressure medications are more effective when taken in the evening [12, 13]. The effects of anesthetics such as neuromuscular blocking agents [14] or local anesthetics [15] or even outcome from anesthesia [16] have been shown to be linked to the circadian system. In fact, the high amount of cycling proteins and physiological functions in our human body rises the question if anesthesia or research might have different outcomes if performed at different time points. Even though it seems logical, no clinical or research study seems to address the impact of circadian rhythms on outcome or results. In a clinical setting we try to be efficient and even have centers where surgeries are performed 24/7. In research, nobody knows if the experiments were conducted in the morning or late at night. Many findings and in particular negative findings could be a result of such an inaccuracy. Hopefully future clinical and basic science studies in anesthesiology and beyond will control for those factors. In fact, many studies might need to be repeated in light of this important but disregarded system: the circadian rhythms, evolved over the last two billion years.

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