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Local Use-Dependent Sleep

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INTRODUCTION

A new view of the brain organization of sleep has initiated a paradigm shift in sleep research. The new paradigm views sleep as an emergent property of the collective output of smaller functional units within the brain [1-4]. State oscillations between two or more patterns of neuronal activity, one exhibiting properties of sleep and another properties of wakefulness, occur within small neuronal networks (also called neuronal assemblies or neuronal groups) such as cortical columns [5]. The sleep-like state of neuronal networks shares many properties of whole organism sleep, including homeostasis, activity-dependence, and altered or impaired functioning in pathological conditions. State oscillations also occur within individual neurons, e.g. up- and down-states, and may contribute to network oscillations [6]. This view of sleep being initiated at a local level in response to local brain activity stands in contrast to the prevailing view that sleep is imposed on the brain by sleep regulatory networks. There are multiple reviews and books devoted to the latter idea [7-11]. In contrast, the local use-dependent view of sleep has yet to be the subject of an integrated journal issue.

The new local sleep paradigm is derived from many disciplines and research approaches. Clinical observations by neurologists indicated that patients behaved at times as if they were partially awake and partially asleep [12]. The developmental literature demonstrated use-dependency of the regional development of EEG patterns [13] and sleep-dependency of local plastic events [14, 15]. The learning and memory literature showed that specific learning-associated neuronal firing patterns are repeated during subsequent sleep in neural structures necessary for learning [16]; these data provide evidence for both use-dependence and local tuning of sleep-related neuronal activity. The comparative animal literature described EEG patterns indicative of half of the brain being asleep and half being awake in marine mammals [17, 18]. Human studies involving either multiple electrode EEG techniques or various imaging methods concluded that within the brain sleep unfolds regionally [19, 20]. Experimental imaging studies suggested that metabolism in specific brain regions during sleep varies in proportion to their metabolic load during prior waking activity [21, 22]. Clinical imaging studies of patients with insomnia indicated parts of the brain were activated while other parts had lower metabolic rates characteristic of sleep [23]. Electrophysiological studies suggested a local source for EEG slow wave activity [24]. Those working on the biochemistry of sleep regulation provided evidence that cellular

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production of substances involved in sleep regulation (e.g., adenosine, tumor necrosis factor) are use-dependent, and that they act to induce regional state-specific EEG patterns in proportion to regionally-driven sleep need [2, 25-28]. Excessive activation of discrete locations within the cerebral cortex during waking results in higher EEG delta wave amplitudes during subsequent sleep in these locations relative to nearby areas [29-31].

Characterization of individual cortical columns using evoked response potentials directly demonstrated that the columns oscillate between states resembling sleep and wakefulness in parallel with changes in blood flow [5]. At the theoretical level, state instability and poor performance associated with sleep deprivation can be viewed as a result of an increasing number of neuronal assemblies switching to sleep-like states and thereby reducing the performance fidelity of multiple assemblies needed for the task at hand [32]. Mathematical modeling efforts have contributed to the idea that whole animal sleep is a self-organizing, emergent property of the collective actions of small units in brain [33] – thereby suggesting that sleep is indeed self-organizing and a property of any viable neuronal network.

The model in which sleep is imposed on the brain by subcortical sleep regulatory centers is of limited utility in explaining many sleep-related phenomena, including homeo-static regulation of sleep slow-wave activity, sleep inertia, parasomnias, sleep loss-induced performance decrements and sleep reorganization after brain lesions. The paradigm represented by the articles in this issue offers testable hypotheses for the mechanisms underlying these phenomena Despite the significant potential of and the extensive experimental support for the new paradigm, and the fact that almost all of those responsible for these developments remain professionally active, there has not been a collection of essays focused on the new paradigm and its clinical and neuro-biological manifestations.

In this issue, many of those who contributed to the foundations of change review their observations within the context of the current literature and reflect on the consequences of their work for clinical and experimental biomedical science.

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