

Spindle Power Is Not Affected after Spontaneous K-Complexes during Human NREM Sleep

Andreas M. Koupparis, Vasileios Kokkinos, George K. Kostopoulos*

Neurophysiology Unit, Department of Physiology, Medical School, University of Patras, Rion, Greece

Abstract

K-complexes and sleep spindles often grouped together characterize the second stage of NREM sleep and interest has been raised on a possible interaction of their underlying mechanisms. The reported inhibition of spindles power for about 15 seconds following evoked K-complexes has implications on their role in arousal. Our objective was to assess this inhibition following spontaneous K-complexes. We used time-frequency analysis of spontaneous K-complexes selected from whole-night EEG recordings of normal subjects. Our results show that spindles are most often observed at the positive phase following the peak of a spontaneous KC (70%). At latencies of 1–3 s following the peak of the K-complex, spindles almost disappear. Compared to long-term effects described for evoked KCs, sleep spindle power is not affected by spontaneous KCs for latencies of 5–15 s. Observation of the recurrence rate of sporadic spindles suggests that the reduction of power at 1–3 s most likely reflects a refractory period of spindles lasting for 1–2 s, rather than an effect of KCs. These results suggest that the mechanisms underlying spontaneous KCs do not affect spindle power as in the case of evoked KCs.

Citation: Koupparis AM, Kokkinos V, Kostopoulos GK (2013) Spindle Power Is Not Affected after Spontaneous K-Complexes during Human NREM Sleep. *PLoS ONE* 8(1): e54343. doi:10.1371/journal.pone.0054343

Editor: Maxim Bazhenov, University of California, Riverside, United States of America

Received: July 6, 2012; **Accepted:** December 12, 2012; **Published:** January 10, 2013

Copyright: © 2013 Koupparis et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Funding: The work was partially funded by the European Commission under the Seventh Framework Programme (FP7/2007-2013) with grant ARMOR, agreement number 287720. Andreas Koupparis has been co-financed by the European Union (European Social Fund – ESF) and Greek national funds through the Operational Program "Education and Lifelong Learning" of the National Strategic Reference Framework (NSRF) – Research Funding Program: Heracleitus II. Investing in knowledge society through the European Social Fund. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Competing Interests: The authors have declared that no competing interests exist.

* E-mail: gkkostop@med.upatras.gr

Introduction

The sleep spindle and the K-complex (KC) are the electroencephalographic (EEG) hallmarks of the second stage of human non-rapid eye movement (NREM) sleep. Defined as a high-voltage biphasic slow wave with a negative phase that may be followed by a positive phase, the KC is one of the most distinguished graphoelements of the EEG [1,2]. The sleep spindle, an oscillatory rhythm (11–15 Hz) of a waxing and waning shape, lasting 0.5–2 s is also a clearly distinguishable EEG event unique to sleep [3]. Fast (~13–15 Hz) and slow (~11–12 Hz) spindles are readily distinguishable with maximal power in centro-parietal and centro-frontal regions respectively [4–6].

A notable observation since the first description of the KC [7] is that it may appear either spontaneously or after a sensory stimulus, in which case it is named 'evoked'. This fact has led to a series of experiments over the decades on a search of its functional significance, with many researchers correlating the appearance of a KC with autonomic alterations and forthcoming arousals [8–12], thus assuming it is an arousing reaction. On the other hand, some suggest that the KC represents a sleep-protecting mechanism averting arousals [2]. Finally, a combined view of KC being a sleep promoting reaction to arousing stimuli seems to gain acceptance [13]. The role of the sleep spindle is also a subject of research since its first description [14] with data supporting its sleep preservation role as an arousal inhibitor [15]. The importance of understanding the mechanisms underlying KCs, spindles and their possible interaction extends also beyond their role in sleep maintenance, as

they have been proposed to be implicated in memory consolidation [16], stroke and spindle-coma [17], schizophrenia [18] and epilepsy [1,2,19,20].

The relationship between KCs and spindles has been described as antagonistic. Administration of benzodiazepines increases spindle appearance and decreases KCs [21–23]. In a period of 10 s before transient arousals, the incidence of spontaneous KCs increases while there is a decrease of both isolated sleep spindles and of spindles associated with KCs [24,25]. Halasz [13] reported a suppression of spindles power for 5–15 s following evoked KCs that were part of a microarousal, thus proposing that these states allow a window of improved sensory inflow at the thalamocortical (TC) circuits while preserving sleep continuity. KC is also seen as the forerunner of delta waves of slow-wave sleep (SWS) and this scheme resembles the reciprocal relationship of sleep spindles and delta waves [3,26]. Curcio et al [27] showed an increase of sleep spindles throughout the night while the occurrence of spontaneous KC decreased. Other studies support independent roles for spindles and KCs. Following stroke spindles disappear while KCs remain [28]. Church et al [29] found that there is no suppression of evoked KC by spindles, a result confirmed by Crowley et al [30]. In the underlying network level, sleep spindles are paced by TC networks whereas KCs by intracortical networks [31], independently from the thalamus [32] (but see Crunelli et al [33] and Bonjean et al [34]).

Kokkinos and Kostopoulos [35] using time-frequency analysis (TFA) showed that fast spindles which happen to coincide with spontaneous KCs are interrupted, during that interruption a slower