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An intra-K-complex oscillation with independent and labile frequency and topography in NREM sleep

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NREM sleep is characterized by K-complexes (KCs), over the negative phase of which we identified brief activity in the theta range. We recorded high resolution EEG of whole-night sleep from seven healthy volunteers and visually identified 2nd and 3rd stage NREM spontaneous KCs. We identified three major categories: (1) KCs without intra-KC-activity (iKCa), (2) KCs with non-oscillatory iKCa, and (3) KCs with oscillatory iKCa. The latter group of KCs with intra-KC-oscillation (iKCo), was clustered according to the duration of the iKCo. iKCa was observed in most KCs (1150/1522, 75%). iKCos with 2, 3, and 4 waves were observed in 52% (786/1522) of KCs in respective rates of 49% (386/786), 44%, and 7%. Successive waves of iKCos showed on average a shift of their maximal amplitude in the anterio-posterior axis, while the average amplitude of the slow KC showed no spatial shift in time. The iKCo spatial shift was accompanied by transient increases in instantaneous frequency from the theta band toward the alpha band, followed by decreases to upper theta. The study shows that the KC is most often concurrently accompanied by an independent brief iKCo exhibiting topographical relocation of amplitude maxima with every consecutive peak and transient increases in frequency. The iKCo features are potentially reflecting arousing processes taking place during the KC.

Keywords: K-complex, NREM sleep, human EEG, theta, alpha

INTRODUCTION

The K-complex (KC) is a major EEG graphoelement characterizing the second stage of the human NREM sleep. By definition, the KC is a biphasic slow wave that stands out of the NREM electroencephalographic background, with a negative phase that may or may not be immediately followed by a positive phase or a sleep spindle (Colrain, 2005; Halász, 2005). The KC was initially described more than 70 years ago by Loomis et al. (1938), but its functional role is still not clearly determined. Yet several of its properties are well-documented: it can be emitted spontaneously as well as be evoked by external stimuli (Loomis et al., 1938; Niiyama et al., 1996), it is exclusive to NREM sleep (Weitzman and Kremen, 1965; Goff et al., 1966), it has a primarily frontal lobe distribution (Davies et al., 1939; Massimini et al., 2004), it is accompanied by autonomic alterations (Roth et al., 1956; Ackner and Pampiglione, 1958; Hornyak et al., 1991; Okada et al., 1991; Takehuchi et al., 1994; Tank et al., 2003), it is a phenomenon independent of sleep spindles (Johnson et al., 1976; Church et al., 1978), its frequency of occurrence is decreased by benzodiazepine administration (Gaillard and Tissot, 1975; Johnson et al., 1976, 1979; Naitoh et al., 1982; Kubicki et al., 1987) and its neuronal generators are cortical and widely, although predominantly frontally, distributed (Velasco et al., 2002; Cash et al., 2009).

The main question regarding the KC along the course of sleep research has been whether it represents a brief hypnagogic or arousing neuronal brain function. It is believed to introduce delta activity into NREM sleep (Halász et al., 1977; Halász, 1981; De Gennaro et al., 2000; De Gennaro and Ferrara, 2003) and for that it is considered to be a sleep-promoting mechanism. In particular, the spontaneous KC is considered to be reacting to unknown endogenous or exogenous stimuli that are not intense enough to provoke an arousal to full wakefulness (Halász et al., 1985). On the other hand, the KC is often followed by arousal- and microarousal-related EEG events (Ehrhart et al., 1981), autonomic alterations (Sforza et al., 2000), as well as movement (MacFarlane et al., 1996); therefore, it is considered by some to be a micro-arousing cortical reaction. As it is commonly agreed that the KC *per se* is unlikely to be responsible for the fluctuations observed in autonomic measurements, another argument has been put forward according to which the KC is a cortical reaction to stimuli that can also cause autonomic reactions, thereby aiming in avoiding cortical awakening, sometimes achieving sleep-protection and sometimes failing to (Colrain, 2005; Halász, 2005). Another theory considers the KC highly correlated to brief (<1 s) cortical depolarization-hyperpolarization oscillations, during which intra-cortical activity takes place as the cortex has been isolated from the environment by thalamic inhibition. Thereby, the KC could represent the transition between a state of neuronal activation (depolarization phase) and a state of rest (hyperpolarization phase) reflected in the KC prominent negative phase (Amzica and Steriade, 2002; Cash et al., 2009).

In a recent work investigating rhythmic activity around and during the KC (Kokkinos and Kostopoulos, 2011), we reported sleep spindle interruption upon coincidental KC appearance and generation of higher spectral frequency sleep spindles toward the