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REVIEW

STATE-DEPENDENT ALPHA PEAK FREQUENCY SHIFTS: EXPERIMENTAL EVIDENCE, POTENTIAL MECHANISMS AND FUNCTIONAL IMPLICATIONS

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Abstract—Neural populations produce complex oscillatory patterns thought to implement brain function. The dominant rhythm in the healthy adult human brain is formed by alpha oscillations with a typical power peak most commonly found between 8 and 12 Hz. This alpha peak frequency has been repeatedly discussed as a highly heritable and stable neurophysiological ''trait'' marker reflecting anatomical properties of the brain, and individuals' general cognitive capacity. However, growing evidence suggests that the alpha peak frequency is highly volatile at shorter time scales, dependent on the individuals' ''state''. Based on the converging experimental and theoretical results from numerous recent studies, here we propose that alpha frequency variability forms the basis of an adaptive mechanism mirroring the activation level of neural populations which has important functional implications. We here integrate experimental and computational perspectives to shed new light on the potential role played by shifts in alpha peak frequency and discuss resulting implications. We further propose a potential mechanism by which alpha oscillations are regulated in a noisy network of spiking neurons in presence of delayed feedback.

Key words: alpha peak frequency, activation state, frequency tuning, network oscillations, information gating, neural computation.

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INTRODUCTION

Alpha activity is one of the most salient dynamical features of both the resting and awake human brain. These pervasive electrical oscillations, most usually found within the 8 to 12 Hz frequency band, have emerged as one of the most robust predictors of brain state. Since their discovery by Hans Berger in 1929 (Berger, 1929), alpha oscillations have been the center of numerous neuroscientific investigations. One of the most consistent observations about alpha oscillations is their sustained variability. Indeed, the frequency of human alpha oscillations have been found to change according to age, cognitive state, sensorimotor processing, sleep and across a wide range of neurological disorders (Uhlhaas and Singer, 2006). To which extent this variability reflects shifts in neural processing states and/or timely transitions in neural sampling strategies is currently poorly understood. A better understanding of the mechanisms involved in shaping the frequency of endogenous alpha oscillations would represent a significant progress in linking macroscopic brain recordings to the dynamics of cortical networks and the underlying computational schemes.

In light of converging experimental and computational results from numerous recent studies, we here wish to link different perspectives into a unified framework. We propose that alpha peak frequency variability does not represent random fluctuations but instead constitutes the basis of an adaptive mechanism mirroring the activation level of neural populations. By adaptive, we mean that the frequency of synchronous neural activity is self-regulated and is tuned autonomously, adjusting to task demands to regulate input and information

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processing. We discuss one well-studied candidate mechanism supporting such frequency regulation in a neural network model with delayed feedback, suggesting that these transitions might be a generic property of cortical networks.

Over the last few years, numerous studies have raised the fascinating prospect of using non-invasive stimulation to manipulate endogenous alpha oscillations in order to alter cognition and alleviate symptoms of neurological disorders. Given that cortical systems possess the intrinsic ability to regulate their peak frequency, we believe it is critical to better understand what these frequency transitions mean in terms of neural dynamics and information processing. By exploring the mechanisms involved, we might be able to devise more accurate control stimulation paradigm and better understand the role of neural oscillations in brain function.

STATE-DEPENDENT ALPHA FREQUENCY TRANSITIONS IN HUMANS

It is well documented in the literature that the resting-state *alpha peak frequency* (APF) can differ remarkably between and within individuals. Specifically, in close analogy to brain volume and general cognitive development, the APF increases from early childhood until adolescence, remains stable during adulthood and then starts to decrease with age and/or manifestation of neurological disorders such as Alzheimer's disease (cf. Klimesch, 1999). Nevertheless, even age-matched healthy individuals exhibit variations in APF with a mean standard deviation of about 1 Hz (reviewed in Klimesch, 1996, 1997). Other neurological conditions associated with slowing of the APF include reduced oxygen supply to the brain such as in cerebral ischemia (Van der Worp et al., 1991) and in carotid artery occlusion (Mosmans et al., 1983) as well as burnout syndrome (van Luijtelaar et al., 2010), cancer-related fatigue (Zimmer et al., 2015) and neurogenic/neuropathic pain (Sarnthein et al., 2006; Boord et al., 2008). However, the APF increases again following carotid endarterectomy (Uclés et al., 1997; Vriens et al., 2000) as well as after neurosurgical pain relief therapy (Sarnthein et al., 2006). The resting state APF is highly heritable (Posthuma et al., 2001; van Beijsterveldt and van Baal, 2002), and it has been shown to qualify as a stable neurophysiological trait marker in healthy younger and older adults (Grandy et al., 2013).

However, growing experimental evidence indicates that substantial APF fluctuations exist at much smaller time scales (e.g. one second), where such fluctuations were found positively correlated with regional cerebral blood flow (rCBF) in a brain network comprising areas that are associated with the modulation of attention and preparedness for external input (Jann et al., 2010). Moreover, a number of studies reported shifts of the APF as a result of an acute intervention across various conditions. For example, Angelakis et al. (2004) observed significant increases in APF immediately after the Digit Span working memory task, however, only for those participants whose APF was lower than the sample median before the task (Angelakis et al., 2004). More recently, Haegens et al. (2014) as well as Maurer et al. (2015) reported a load-dependent acceleration of the APF during performance of a N-back and a modified Sternberg task, respectively (Haegens et al., 2014; Maurer et al., 2015). In addition, Gutmann et al. (2015) found a significant increase of the resting state APF following a strenuous bout of cycling exercise whereas following moderate intensity exercise, the change of APF was substantially smaller, and not significant (Gutmann et al., 2015). This indicates the extent of physiological changes induced by physical exercise, and thus, most probably, the input to the brain, is associated with the extent of APF acceleration. In a similar manner, Hülsdünker et al. (2016) reported increases in APF during more demanding balance task performance (e.g. unipedal vs. bipedal balancing) (Hülsdünker et al., 2016). Moreover, in this study a significant positive correlation was found between APF and the amount of postural sway probably suggesting that the APF increases with increased allocation of attentional resources as well as increased somatosensory input to the brain as a consequence of postural instability. The APF was also found to increase during tonic noxious thermal pain stimulation (Nir et al., 2010) as well as after acute administration of nicotine (Lindgren et al., 1999), caffeine (Tiffin et al., 1995; Bchir et al., 2006) and buflomedil – a vasoactive drug (Saletu et al., 1984). However, and this is important in view of the computational predictions (see below), the change of APF is bidirectional depending on the individual's state. Specifically, reductions of the APF were observed during the ideational reproduction of sorrow and fear emotions whereas emotions of joy and anger induced a shift of the APF in the opposite direction (Kostyunina and Kulikov, 1996). Furthermore, significant deceleration of the APF was reported during Qi Gong (Zhang et al., 1988) and meditation state (Saggar et al., 2012). Moreover, the APF was positively correlated with the Coma-Recovery Scale - Revised (CRS-R) score in patients suffering from disorders of consciousness. That is, the lower the total CRS-R score and thus, the expected degree of consciousness, the lower the APF (Lechinger et al., 2013). Interestingly, the APF shifts reported in coma patients are substantially different from those reported during sleep (Lechinger et al., 2015) or anesthesia (cf. Purdon et al., 2015) - which also display a slowing down of neural activity - despite the fact that the reduced degree of consciousness is common for all these situations.

The cumulative pattern of experimental results clearly indicates that the task-/state-dependent change in APF is a widespread phenomenon not limited to specific types of tasks. Moreover, a number of studies suggest the APF changes as a function of task demands or input intensity. This, as well as the general concept of the proposed APF modulation mechanism is illustrated in Figs. 1 and 2, respectively. In a similar way as heart rate, intraindividual shifts may be interpreted in terms of task-/state-dependent adaptations whereas interindividual differences may reflect differences in biology, and with respect to alpha, differences in brain connectivity (Valdés-Hernández et al., 2010).