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A SHORT REVIEW OF ALPHA ACTIVITY IN COGNITIVE PROCESSES AND IN COGNITIVE IMPAIRMENT

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ABSTRACT

Aim of the report

In the companion report (Başar, this volume), the physiological fundaments of alpha activity in integrative brain function are described. The present report is a review of the significant role of alpha activity in memory and cognitive processes in healthy subjects, and in cognitive impairment. The role of neurotransmitters is also described, briefly, in this context.

Towards an Understanding of Brain Alpha

Despite numerous experimental studies, it is indicated that the presented results are only appropriate to establish an ensemble of reasonings and suggestions for analyzing "alphas" in the *whole brain*. In turn, in the near future, these *reasonings and suggestions* may serve (or are indispensable to serve) as fundaments of more general and tenable hypotheses on the genesis and function of "alphas".

Keywords: EEG, Alpha, Evoked Alpha, Event Related Alpha, Event Related Oscillations, Memory, Cognitive Impairment, Emotion, Pre-stimulus alpha, Alzheimer's Disease, Bipolar Disorder, Schizophrenia, Evoked Coherences, Event Related Coherences

1. ALPHA IN FUNCTIONAL COGNITIVE STATES AND MEMORY

The statements "*alpha is noise*" or "*alpha oscillations manifest the idling of the brain*" were highly influential in the neuroscience literature until the mid-1990s, despite the resurgent interest in brain oscillations in the study of brain function. Most oscillation-related studies of cognitive processes focused on analysis of the gamma band. Since the focusing of studies to the gamma band for understanding of brain function is highly limited, a conference on functional correlates of alpha activity was organized in Lübeck, Germany, and a triple-special issue of the International Journal of Psychophysiology was devoted to the results of this conference. The proceedings of this conference were edited by Başar et al. (1997). The importance of the rationale for attacking problems of alpha-oscillations was explained in the preface (Başar, 1997). The results in that special issue spanned from the cellular level up to cognitive process, which were scarcely published previously; Thereafter, the number of reports on the cognitive correlates of alpha activity increased greatly. In particular, the results of the Klimesch group contributed greatly to this trend. Nevertheless, we intend to explain that alpha functionality and models of alpha activity should not be limited to cognitive processes and short-term memories.

Accordingly, before considering and/or describing hypotheses related to cognitive correlates of alpha and alpha-related memory, we briefly describe some general principles related to memory. Further, before attacking the topics of cognitive processes and relevant pathology, it is necessary to consider the results in light of reasoning related to basic functions and the physiologic framework of the alpha processes described in the companion report. We intend to carefully formulate that all reasoning on alpha and memory should be discussed within the context of these frameworks.

It is also important to briefly describe some important theories on memory for the embedding of alpha oscillations within these frameworks.

1.1. What are Bottom-Up and Top-Down Processing?

These terms are employed in neuroscience, cognitive neuroscience and cognitive psychology to discuss the flow of information in processing. Typically, sensory input is considered "*down*", and higher cognitive processes, which have more information from other sources, are considered "*up*". A *bottom-up* process is characterized by an absence of higher-level direction in sensory processing, whereas a *top-down* process is characterized by higher-level direction of sensory processing by cognition, such as goals or *targets*. In terms of cognitive physiology, certain cognitive processes, such as fast reactions or rapid visual identification, are considered bottom-up processes because they rely primarily on sensory information, whereas processes such as *motor* control and *directed attention* are considered top-down. Neurologically speaking, some areas of the brain, such as area V1, mostly have bottom-up connections. Other areas, such as the *fusiform gyrus*, have inputs from higher brain areas and are considered to have top-down influence.

The study of *visual attention* provides an example. If the attention is drawn to a flower in a field, it may be because the color or the shape of the flower is visually salient. The information which causes one to attend to the flower comes in a bottom-up fashion — the attention is not contingent upon knowledge of the flower; the outside stimulus alone was sufficient. Contrast this situation with that in which one is looking for a particular flower, of which we have a prior representation. When we see the object we are looking for, it is salient, but objects not matching our representation are rejected. This is an example of the use of *top-down* information. The study by Strüber and Hermann (2002) could be an example of bottom up processes. These authors analyzed MEG alpha activity during presentation of ambiguous figures and they have showed that the endogenous of alpha activity displayed a decrease starting in the time interval preceding the reversal. Accordingly, the authors concluded that this time course of the endogenous alpha activity is consistent with a bottom up approach to figure reversals.

1.2. Memory Function according to Fuster, Baddeley, Desimone and Goldman-Rakich: Categorization of Memory

a) Phyletic Memory

Perceiving refers to the classification of objects by activation of the associative networks that represent them in memory. It is reasonable to assume, as Hayek (1952) did, that, to a large extent, memory and perception share the same cortical networks, neurons and connections. To understand the formation and topography of memory, it is useful to think that the reaction ability of the primary- sensory and motor areas of the cortex is called *phyletic memory* or *memory of the species (Fuster, 1995).* The structure of primary sensory and motor cortices may be considered as a fund of memories that the species has acquired during evolution. We can call it memory because, like personal memory, it is information that has been acquired and stored, and can be retrieved (recalled) by sensory stimuli or the need to act.

b) Perceptual Memory

Perceptual memory is memory acquired through the senses. It comprises all that is commonly understood as personal memory and knowledge, i.e. the representation of events, objects, persons, animals, facts, names and concepts. From the hierarchical viewpoint, *memories* of elementary sensations are at the bottom; at the top tier are abstract concepts that, although originally acquired by sensory experience, have become independent from it in cognitive operations.

c) Procedural Learning

Procedural memory is the representation of a series of actions or perceptual processing functions that occur unconsciously and, with repetition, typically result in increased speed or accuracy. This refers to the acquisition of skills, whether perceptual–motor, such as those of riding a bicycle or driving a car; or cognitive, such as in skilled reading or problem-solving. Such acquired skills clearly comprise an important area of learning and do, of course, represent the archetypal example of procedural learning—learning *how* rather than learning *that* (Eichenbaum, 2000).

Skills can be divided into two types: *continuous*, in which each component of the skill serves as a cue to the next, as in cycling or steering a car; and *discontinuous*, in which a series of discrete stimulus-response links are involved, as in typing.

1.2.1. Structure of Memory

Another important categorization of memories (or memory states) is the distinction between *"implicite and explicite"*. The view of Squire (1992) distinguishes between *declarative* and *non-declarative* memory, terms which more-or-less map onto the earlier terms of implicit and explicit (Fig. 1).

An early distinction was made between *procedural* and *declarative* learning, with procedural learning representing the acquisition of skills, "*learning how*", while declarative learning involves the acquisition of facts, "*learning that*" (Squire, 1992; Baddeley, 1996). However, while many of the preserved learning capacities could be regarded as skills, it seemed to be stretching the term to regard conditioning, or indeed stem completion, as genuinely procedural.

According to Baddeley (1996), it has become increasingly clear that memory comprises not a single system, but rather an **alliance of interrelated subsystems**. Empirical evidence for the distinction between long- and short-term memories began to emerge in the 1960s.From Fuster's (1997) point of view, *memory reflects* a distributed property of cortical systems. An important part of higher nervous function, such as perception, recognition, language, planning, problem-solving and decision-making, is interwoven with memory. Furthermore, memory is a property of the neurobiological systems it serves, and is inseparable from their other functions. By surveying the data presented in this section, it can be hypothesized that the selectively distributed oscillatory systems (or networks) may provide a general communication framework and can be a useful concept for functional mapping of the brain (Mesulam, 1990, 1994; Başar, 2004; Schürmann et al., 1995, 1997; Başar-Eroğlu et al., 1991).

1.3. Relevance of Alpha Cognitive Components

Cognitive targets significantly influence alpha responses in P300: Using an oddball paradigm, *prolonged* event-related alpha oscillations up to 400ms were observed by Stampfer and Başar (1985), Başar and Stampfer (1985) and later by Kolev et al. (1999), with a clear demonstration by means of single sweep analysis. Yordanova and Kolev (1998) assessed the effect of auditory oddball task processing on slow (7–10 Hz) and fast (10–14 Hz) alpha activity from the P300 latency range. The results demonstrated that larger and more synchronized phase-locked fast alpha components at anterior (frontal-central) locations, with reduced non-phase-locked slow alpha responses at the parietal site, were produced by targets relative to non-targets. As the simultaneously-recorded P300 and alpha activity manifested a similar sensitivity to the oddball task, event-related alpha appears to be functionally associated with the cognitive processing demands eliciting P300. Also, there is evidence for the functional involvement of frontally-synchronized and enhanced alpha oscillations in task processing.

Memory related, event-related alpha oscillations can be observed in well-trained subjects one second before an expected target (Maltseva et al., 2000). Results from the Klimesch group demonstrate that alpha activity is strongly correlated with working memory and probably with long-term memory engrams.

The co-existence of evoked alpha oscillations with alpha blocking and event-related desynchronization (Pfurtscheller et al., 1997) hints at *multiple processes* being reflected in alpha oscillations. Examples of such co-existence are evident in earlier measurements, where high-amplitude spontaneous alpha activity coincided with alpha blocking, while low-amplitude alpha preceded EPs of high amplitude (Başar, 1998; Klimesch et al., 2000). In more recent studies, Klimesch et al. (2000) showed a plausible superposition of several types of alpha oscillations together in a schematic form. Furthermore, Krause et al. (2001) also reported event-related synchronizations and desynchronization together.

Makeig et al. (2002) published a study relevant to the question of whether the averaged evoked potential (EP) is a tiny signal added to otherwise non-stimulus-related EEG oscillations, or whether the EP is a re-organization of ongoing EEG oscillations. Makeig's data, obtained from 15 subjects with approximately 3,000 trials per subject, substantially extended earlier experimental evidence for the role of phase re-ordering in EP generation. The experimental designs created by various research groups (Burgess and Gruzelier, 2000; Egner and Gruzelier, 2001; Haenschel et al., 2000; Klimesch, 1999; Klimesch et al., 1994) add to the general framework of function-related oscillations. On the other hand, Mazheri and Jensen (2006) showed that that in single trials the alpha oscillations after visual stimuli preserve their phase relationship with respect to the phase before the stimuli. The authors conclude that, their finding argues against phase-resetting of ongoing oscillations as being responsible for visually evoked responses. Min et al. (2007) investigated the relationship between event related alpha activity and prestimulus ongoing alpha activity during application of visual discrimination task. These authors showed that all groups exhibited event related increase in phase-locked alpha activity. Furthermore, only individuals with sustained prestimulus alpha activity showed alpha blocking. In contrast, individuals without observable prestimulus total alpha activity showed a increase of phase locked and non phase locked activity. Accordingly, the authors concluded that both phase resetting and additive power contribute to the generation ERPs.

Although the relationship of alpha activity to dynamic memory and working memory was tentatively hypothesized by Başar and Stampfer (1985), the research of the Klimesch group (Klimesch et al., 1997, 2000, 2006, 2007) showed the possibility of differentiating the role of alpha and theta oscillatory activity during memory tasks. The results from this group support the hypothesis that ERPs can be understood and described in terms of the superposition of several event-related oscillations recorded in various structures (Klimesch et al., 2000; Doppelmayr et al., 2000). Moreover, their experiments include memory tasks differentiating oscillatory responses of human subjects between good and bad memory performers.

Busch and Herrmann (2003) analyzed 10 Hz oscillations upon application of a short term memory task. Their results shoed that task induced alpha oscillations increased during the delay phase of a delayed matching-to-sample task when the number of features increased that had to be memorized. Furthermore these authors stated that their results seem to add to the evidence that the alpha activity represents more than just a state of cortical inactivity. Herrmann et al. (2004) compared alpha responses between a perception and a memory condition. Increased total alpha activity was found in the retention interval for the memory as compared to the perception condition. Evoked alpha activity, however, did not differentiate between memory and perception conditions but, instead, was increased for the more complex condition of processing non-Kanizsa figures as compared to Kanizsa figures. Thus, the results of these authors described a functional differentiation between evoked and total alpha activity. In their paradigm, alpha phase-locking seemed to be influenced mainly by task complexity, whereas alpha amplitude clearly reflected memory demands.

1.4. Extensions to the Role of Alpha in Cognitive Processes. What Does Time Inhibition Mean?

In the previous section, we described definitions of bottom-up and top-down processes in the brain, together with relevant theories related to memory in the human brain. The following section discusses a number of publications from the last decade, which placed great emphasis on the role of alpha activity in top-down processing. The theories presented by Fuster (1995, 1997), Baddeley et al. (1995), Goldman-Rakic (1996) and Larry Squire (1992) clearly explain the role of inborn phyletic memory (iconic, echoic) and also that memory states are inseparable from basic brain functions. Besides remembering, memory functioning also comprehends processes of sensation, perception and learning. Accordingly, memory theories manifested in brain oscillations could not be considered as pure top-down processes; bottom-up processes do occur in parallel or as serial processing. Sensory alpha responses in humans have been described by several authors, starting with Başar (1972), Spekreijse et al. (1972), Başar et al. (1975a,b,c), and Başar (1980); and in the human brain by Başar (1976). In terms of the most fundamental findings, Dinse et al. (1997) and Dudkin et al. (1978) described visual-evoked oscillations at the cellular level; the 10-Hz responses demonstrated by these authors were triggered by pure light signals and did not include cognitive tasks. Although the association of alpha activity with working memory was first described by Başar and Stampfer (1985) and Stampfer and Başar (1985), more comprehensive and detailed studies of brain oscillations and memory were achieved in a long series of papers by the Klimesch group, firstly emphasizing differences between good and bad memory performers by means of oscillations. Recently, Klimesch et al. (2007) launched a hypothesis related to the "inhibition timing in alpha oscillations", which suggested that the event-related alpha response can be described solely in terms of suppression or event-related synchronization. Nevertheless, the traditional position (described above, in Sections 1 and 2), is the description of alpha sensory response and event-related response following Adrian (1941) and Bishop (1953), who measured alpha responses upon pure sensory stimulation.

Klimesch (1996) and Klimesch et al. (1993, 1997) claimed that the vast majority of experiments correlate alpha with cognitive performance. The general view here is that, in comparison to a resting period, task demands tend to attenuate or desynchronize alpha rhythms (Berger, 1929). According to Klimesch et al. (2007), the traditional theory is that the event-related alpha response can solely be described in terms of suppression or event-related desynchronization (ERD). These authors also indicate that, under certain conditions, alpha responds reliably, with an increase in amplitudes (event-related synchronization or ERS). ERS is elicited in situations where subjects withhold or control the execution of a response, and is obtained over sites that are probably under, or exert top-down, inhibitory control process. Thus, the authors assume that alpha ERS reflects top-down, inhibitory control processes. Their general conclusion is that alpha ERS plays an active role in the inhibitory control and timing of cortical processing, whereas ERD reflects the gradual release of inhibition associated with the emergence of complex, spreading activation processes. Supporting the Klimesch's theory, Handel et al. (2011) analyzed alpha activity upon visual stimuli presented to the left and right visual hemifields. These authors showed that occipital alpha power was higher contralateral to the unattended side than to the attended side.

Several authors have provided experimental and theoretical support for the hypothesis of Klimesch and co-workers; however, there are also critics of the inhibition theory. Knyazev et al. (2006) explained the essential doubts as follows: "*The idea of inhibitory function for alpha synchronization is appealing but it raises some doubts. First, it is not clear how the same mechanism might be linked with perceptual activation, as in the case of phase-locked evoked alpha oscillations described by Başar (1998, 1999), and perceptual inhibition (as proposed for event-related alpha synchronization, ERS). Further, if ERS served a function of selective attention (e.g. inhibition of non-task-relevant perception), one would expect that relatively small cortical areas within a task-relevant zone would show ERD, whereas larger cortical areas, which are not related to the task processing, would show ERS; actually the opposite applies: Alpha ERD is usually more pronounced and widespread during first presentations of a signal or a task, and is stronger during more complex tasks compared to the relatively simple ones (Neubauer et al., 1999). Such observations are difficult to reconcile with the idea of lateral inhibition as a function of ERS.*"

Knyazev et al. (2006) further indicates the relevance of background activity: "*Owing to extensive studies by Başar (1998, 1999) as well as other authors, a considerable body of knowledge has been accumulated, indicating that, depending on background activity, different reactions of EEG bands could be observed. According to the concept demonstrated by several authors, the ongoing EEG determines (controls) evoked activity*".

Compared to the abundance of experiments dealing with alpha power measurements, relatively few studies focused on task-related shifts in alpha frequency. The experiments by Osaka (1984) showed that only for difficult but not for easy tasks, alpha frequency increases selectively in the hemisphere that is dominant for a particular task.

EEG signals were recorded by Klimesch et al. (1993) from subjects performing a modified version of Schneider and Shiffrin’s memory-search paradigm in order to test whether individual alpha frequency (IAF) is related to memory performance and/or attentional demands. Their results showed that memory performance had a strong effect on individual alpha frequency. Compared to a resting period, the difference in individual alpha frequency between age-matched *good* and *bad memory performers* reached a maximum when subjects were actually retrieving information from their memory. During retrieval, the alpha frequency of good performers was 1.25 Hz higher than for bad performers. The results of amplitude analyses further demonstrate that, during retrieval, alpha desynchronization is more pronounced for bad performers than for good performers. The findings of Klimesch (1996) and Başar et al. (1989) on dynamic memory demonstrate that alpha activity is strongly correlated with working memory and probably with long-term memory engrams (for Klimesch’s interpretation, see also Başar, 2011, Chapter 7).

1.5. What Evidence should be Considered before Launching Hypothesis

The following section includes some critical remarks related to the newly formulated theories or strong statements presented by some authors.

(1) The review by Ward (2003) summarized the recent evidence that synchronous neural oscillations reveal much about the origin and nature of cognitive processes such as memory, attention and consciousness; and that memory processes are most closely related to theta and gamma rhythms, whereas attention seems closely associated with alpha and gamma rhythms. These conclusions are not in accordance with the fundamental views of Fuster (1995, 1997), Baddeley (1996), Goldman-Rakic (1996) and Desimone (1996), who demonstrated that processes of memory and attention are inseparable. This discordance is also contained in the Time Inhibition Hypothesis by Klimesch and coworkers.

(2) Klimesch et al. (2007), and all other authors supporting the hypothesis by Klimesch, omitted the important relationship between pre-stimulus activity and event-related

oscillations in their model. Several authors demonstrated that: the degree of responsiveness in the alpha frequency range is proportional to the amplitude of pre-stimulus alpha activity; in cases where no alpha activity is recorded in prestimulus EEG, desynchronization does not occur (Rahn and Başar, 1993a, b; Stampfer and Başar, 1985; Brandt, 1997; Barry et al., 2006).

(3) The relevant studies of Rémond and Lesevre (1967) should be taken into account, because event-related synchronization and desynchronization is a function of the phase angle of the alpha oscillation at the moment of a flash stimulation. Accordingly, the occurrence of desynchronization can be partly described as an event that is strongly dependent on the state of alpha at the time of the stimulation. The degree of responsiveness depends on the amplitude and phase angle in the prestimulus activity. Unfortunately, interpretations of the relevant and careful analyses by Rémond's group, reflecting an important neurophysiological process, are not taken into account by cognitive validations related to alpha ERD.

(4) Further, during an experiment in a dimly illuminated room, the subjects do not show spontaneous alpha activity and, following each single stimulation, huge alpha response oscillations were observed (Başar et al., 1976).

(5) The child brain does not show alpha activity until the age of three years and, accordingly, alpha desynchronization cannot be observed during a cognitive process in children (see section 7 of companion report by Başar, this issue).

(6) Neither is it possible to observe alpha desynchronization in pathologies where no spontaneous alpha is observed, such as in bipolar disorder.

(7) Until 50 years of age, frontal lobes have poor alpha activity in comparison to posterior recordings. Accordingly, the entire cortex cannot be included in the inhibition timing hypothesis.

(8) By using a measure termed the phase-preservation index, Mazaheri and Jensen (2006) investigated the phase of oscillatory alpha activity (8–13 Hz) before and after stimulus. They found that, in single trials, the alpha oscillations after visual stimuli preserve their phase relationship with respect to the phase prior to the stimuli. This finding argues against phase-resetting of ongoing oscillations being responsible for visually-evoked responses. The event-related field can be explained primarily by stimulus-locked activity in the band that is absent before the stimulus. The authors conclude that different neuronal events are responsible for generating the ongoing oscillations and the visually-evoked responses.

(9) According to Grey Walter (The Living Brain, 1953), studies of large subject groups show there are alpha-type subjects and non-alpha-type subjects. In non-alpha types, alpha desynchronization can in no way be observed.

(10) The *alpha prolongation* during working memory measurements can be also considered by interpreting the role of activity during cognitive processes (Stampfer and Başar, 1985; Öniz and Başar, 2009).

(11) Studies related to excitation or inhibition at the single cell level should be taken into account before pronouncing hypotheses on enhanced EEG responses and inhibition (see Dinse et al., 1991, 1997; Türker and Powers, 2005.)

According to the ten objections described above, the reliability of the inhibition timing hypothesis is limited only to a small percentage of recordings. More extended analyses are needed before pronouncing new hypotheses also besides the time inhibition hypothesis.

2. EVENT-RELATED ALPHA IN EMOTION STUDIES AND ANALYSIS OF COMPLEX SIGNALS

It is clear that the brain can perform a number of more difficult differentiations than those related to simple light, simple auditory signals and oddball strategy. We can differentiate a sea landscape from a mountain landscape; classical music from jazz music; a table from a tree. Recognition of known and unknown faces is the basic step. However, the task of face recognition also includes the recognition of facial expressions. In the analysis of facial expressions, we also confront another task or, as Mark Solms and Oliver Turnbull (2002) discusses, we include in our analysis the sixth sense: *emotions*. According to James (1890), emotions are cognitive responses to information from the periphery. According to Solms and Turnbull (2002), emotion is akin to a *sensory modality that provides information about the current state of body self, as opposed to the state of the object world. "Emotion" is the aspect of consciousness that is left if all externally derived contents are removed."*

Le Doux (1999) proposed that emotions or feelings are *consciousness* of *unconscious processes*. However, he states that, despite millennia of preoccupation with every facet of human emotion, we are still far from explaining, in a rigorous physiological sense, this part of our mental experience. According to Damasio (1994, page 139), "*Emotion is the combination of a mental evaluative process, simple or complex, with dispositional responses to that process, mostly toward the body proper, resulting in an emotional body state, but also toward the brain itself, resulting in additional mental changes."*

Panksepp (2005) defined the term "*Emotion*" as the 'umbrella' concept that includes affective, cognitive, behavioral, expressive, and a host of physiological changes. Furthermore, Panksepp (2005) described "*Affect"* as a subjective experiential-feeling component, and stated that emotional affects are closely linked to internal brain action states, triggered typically by environmental events. In the literature, "affect" was described in terms of valence (positive and negative affects) and arousal (how intense are the feelings) Panksepp (2005).

In the EEG literature, emotional processes and alpha oscillations have mostly been studied by analyzing the resting state frontal alpha asymmetry, starting with the work of Davidson et al. (1979). Since that time, many studies have analyzed and discussed frontal alpha asymmetry. In several parts of the present review, and in Başar, (companion report, this issue), we have also briefly discussed spontaneous alpha activity in children, elderly subjects and in different brain pathologies. We recommend the reviews of Davidson (2003, 2004) for further information on frontal resting alpha asymmetry and emotional processes.

As Knyazev et al. (2006) mentioned, there is evidence that alpha oscillations are enhanced in anxious individuals, particularly in an anxiogenic environment (Bell et al., 1998; Herrmann and Winterer, 1996; Knyazev et al., 2002, 2003, 2004; Knyazev and Slobodskaya, 2003). This enhancement has been interpreted as a sign of increased readiness of the alpha system for information processing (Knyazev and Slobodskaya, 2003).

Predictions derived from the inhibition (Klimesch, 1999; Klimesch et al., 2007) and alertness hypotheses (Başar, 1998, 1999) were tested by Knyazev et al. (2006) during presentation of acoustic stimuli (tone 1000 Hz) and neutral words to 30 males (18–25 years) with different levels of trait anxiety. On the whole, predictions derived from the inhibition theory were not confirmed, and the findings corresponded more closely to the alertness hypothesis. High-anxiety subjects showed higher alpha power during reference interval, simultaneously with higher magnitude of event-related desynchronization and higher amplitude of phase-locked alpha responses.

Aftanas et al. (2002) analyzed event-related desynchronization ERD, and synchronization ERS in alpha-1 (6.21–8.28), alpha-2 (8.28–10.35) and alpha-3 (10.35–12.46) frequency bands in response to International Affective Picture System (IAPS) stimuli with low, moderate and high arousal LA, MA and HA content. The MA and HA vs. LA stimuli yielded greater alpha-1 synchronization, predominantly over occipital leads. Furthermore, these authors reported that, in the alpha-3 band, HA stimuli induce a lateralized time-dependent power increase over anterior leads of the left hemisphere.

Güntekin and Başar (2007) analyzed the event-related alpha oscillations in response to emotional facial expressions (“*angry”*, “*happy”* and “*neutral*”). They reported that the amplitude of alpha responses was significantly higher upon angry face stimulation than during happy face stimulation at posterior locations (specifically T_5, P_3 and O_2).

The above-mentioned studies of *event-related alpha oscillations* in response to emotional processes demonstrate that event-related alpha oscillations are increased upon presentation of different emotional stimuli. On the other hand, Balconi et al. (2009a, b) studied the effect of subjective evaluation and of BIS/BAS (Behavioral Inhibition and Activation System) differences on psycho-physiological and brain oscillation measures in response to pleasant/unpleasant and high/low arousing stimuli. These authors reported decreased alpha power for positive, negative and arousing emotions in comparison to neutral stimuli. Balconi and Mazza (2009) analyzed alpha brain oscillation modulation in response to masked emotional facial expressions. The authors reported that desynchronization of alpha was correlated to higher BIS measures in the right-frontal side. Furthermore, desynchronization of alpha was correlated with angry and surprised facial expressions.

It should also be noted that all of these studies used different methodologies (stimuli type, EEG analyzes). Further research is needed to achieve more congruent results on emotional processes and event-related alpha oscillations.

3. ALPHA IN COGNITIVE IMPAIRMENT

To date, many signal-processing techniques have been utilized to reveal pathological changes in spontaneous EEG associated with different brain pathologies. Spontaneous EEG Alpha activity was found to be lower in schizophrenia (Itil et al., 1972, 1974; Iacona, 1982; Miyauchi et al., 1990; Sponheim et al., 1994, 2000; Alfimova and Uvarova, 2008) and in Alzheimer’s disease (Locatelli et al., 1998; Dunkin et al., 1994; Leuchter et al., 1987; Adler et al., 2003; Rossini et al., 2007; Babiloni et al., 2004, 2009a, b). Reduced alpha activity was reported in bipolar patients with psychotic characteristics in comparison to healthy controls (Clementz et al., 1994). Most recently, Başar et al. (2012b) reported that drug-free euthymic bipolar patients showed greatly reduced spontaneous EEG alpha activity; and also greatly reduced evoked alpha response upon stimulation with basic visual signal. These results on bipolar disorders serve to indicate that such findings may serve, in future, as neurophysiologic markers for distinguishing the results between other pathologies. In future, changes in neurotransmitter release in pathologies will be compared in parallel with changes in oscillatory activities. This type of analysis can provide great insight into the electrophysiological/biochemical fundaments of oscillations. Compare the results of Whittington et al. (2000) for the relationship between GABA and gamma activity.

Figure 2 A represents the grand averages of power spectra of eighteen healthy and eighteen euthymic subjects in the alpha frequency range during an eyes-closed recording session at occipital locations (O_1, O_z, and O_2). While the power spectrum of the alpha frequency range reached 4.80 μV^2 for O_1; 4.0 μV^2 for O_z and 4.50 μV^2 for O_2 electrode in healthy controls, it remained at 1.0 μV^2 across all occipital electrodes in the euthymic patients (Başar et al., 2012b). Figure 2 B represents the grand average of the evoked response power spectra for eighteen healthy and eighteen euthymic subjects in the alpha frequency range upon application of simple light stimuli (for O_1, O_z, and O_2 electrodes). The alpha frequency power spectrum of evoked response reached 0.04 μV^2 in healthy controls, whereas that of euthymic patients only reached 0.015 μV^2.

Previous analysis of alpha activity in different pathologies was based mostly on spontaneous EEG. Within the literature, analysis of evoked- or event-related alpha activity is rare compared to analysis of spontaneous alpha activity. In these publications, evoked- and event-related alpha responses in different pathologies were analyzed using the methods of evoked-event-related power, event-related synchronization (ERS), event-related desynchronization (ERD), evoked-event-related coherence, phase-locking analysis, time frequency analysis, and peak-to-peak amplitudes of averaged- and single-trial alpha responses.

In Alzheimer studies, several authors reported smaller evoked- or event-related coherence in comparison to healthy controls, independent of the stimulus type (Hogan et al., 2003; Kikuchi et al., 2002; Zeng-Yan, 2005). Güntekin et al. (2008) and Başar et al. (2010) reported reduced event-related coherence upon stimulation of visual target stimuli only in unmedicated Alzheimer patients but not in medicated Alzheimer patients.

Euthymic bipolar patients were also reported to have lower alpha response amplitudes in a basic visual paradigm (Başar et al., 2012b). Furthermore, bipolar patients have lower alpha amplitudes, even during manic stage, upon stimulation of visual cognitive paradigm (Özerdem et al., 2008). In contrast, Pin-Shiuan Lee et al. (2010) reported increased alpha response in bipolar patients compared to healthy controls upon stimulation of an emotional paradigm. This ambiguity is important to show how neurophysiologic processes can be influenced by emotions, especially in affective disorders.

3.1. Spontaneous alpha activity, Evoked/Event Related Alpha Response in Schizophrenia patients

We have encountered around ten reviews of evoked/event-related oscillations in schizophrenia patients (Uhlhaas et al., 2008; Başar and Güntekin, 2008; 2012; Haenshcel and Linden, 2011; Brenner et al., 2009; Herrmann and Demiralp, 2005; Lee et al., 2003a; Luck et al., 2011; Sun et al., 2011; Uhlhaas and Singer, 2010; Schnitzler and Gross, 2005). In these reviews, the authors mostly reviewed research on gamma response oscillations in schizophrenia. On the other hand, the studies analyzing alpha response oscillations upon stimulation of different paradigms in schizophrenia patients increased in the recent years..

Spontaneous alpha activity and visual steady-state alpha responses were reported to be reduced in schizophrenia patients compared to healthy controls (Alfimova and Uvarova, 2008; Iacono, 1982, Jin et al. 1990, 1995, 1997, 2000; Itil et al., 1972, 1974; Miyauchi et al., 1990; Rice et al., 1989; Sponheim et al., 1994, 2000; Wada et al., 1995). However, the results for evoked/event-related alpha responses show contradictory results in working memory paradigms. Başar-Eroğlu et al. (2008) reported that neither the amplitude enhancement after stimulus onset nor the inter-trial coherence was generally reduced in patients upon application of a visual oddball paradigm. Later, in a different paradigm, Başar Eroğlu et al. (2009) showed that amplitudes from patients were reduced at Fz and Cz locations only for the early time window (0–250 ms) upon non-target stimuli of auditory continuous performance task. Consistent with the results of Başar-Eroğlu et al. (2009), Koh et al. (2011) reported that alpha inter-trial phase coherence was lower in schizophrenia patients than ultra-high risk subjects, and lower in ultra-high-risk subjects than normal control subjects upon application of an auditory oddball paradigm. On the other hand, Haenschel et al. (2010) demonstrated that alpha phase locking was generally reduced in SZ compared to healthy controls upon delayed discrimination task.

To our knowledge, the first study of visual steady-state responses in schizophrenia patients was conducted by Rice et al. (1989). These authors reported that subjects with schizophrenia exhibited reduced power in the alpha frequency range upon application of periodic photic stimuli. The results of Rice et al. (1989) were subsequently supported by those of Jin et al. (1990, 1995, 1997) and Wada et al. (1995). Jin et al. (1995) showed that visual steady-state response reduction in schizophrenia occurred at higher alpha frequencies (12.5 Hz) but not at lower alpha frequencies (9.375 Hz). Further, these authors reported that group differences were primarily located in the mid-frontal, central and parietal areas; Temporal and lateral frontal lobe alpha remained the same in the two groups. Jin et al. (2000) later reported that schizophrenia subjects showed reduced power at 10, 11 and 12 Hz in all regions except centro-temporal regions when evaluating the harmonics in the alpha frequency range. Clementz et al. (2008) presented a visual target detection task and reported that, for both schizophrenia and healthy subjects, attending to specific parts of the attended image enhanced brain activity related to attended bars, and reduced activity evoked by unattended bars.

Krishnan et al. (2005) evaluated the visual steady-state response for seven different frequencies of stimulation (4, 8, 17, 20, 23, 30, and 40 Hz) using a sinusoidally-modulated high-luminance stimulus. These authors found that schizophrenia subjects showed reduced signal power compared to healthy control subjects at higher frequencies (above 17 Hz), but not at 4 and 8 Hz in the occipital region.

White et al. (2010) analyzed evoked alpha and gamma power in schizophrenia patients upon application of vibrotactile somatosensory task. The authors reported that, in schizophrenia patients, the strongest component had low alpha power and activity was limited mainly to somatosensory regions.

Ramos-Loyo et al. (2009) evaluated event-related oscillations during emotional recognition of happiness and fear compared to facial identity recognition in schizophrenic patients versus healthy controls. Subjects performed three oddball paradigm tasks, evaluating face identity recognition and facial emotional recognition of happiness and fear. The authors analyzed the event-related theta and alpha oscillations for each task and reported that theta oscillations showed significantly lower RMS values in schizophrenia patients between 250 and 500 ms post-stimuli in frontal and central regions.

Haenschel et al. (2009) demonstrated that patients showed reduced evoked theta, alpha, and beta oscillatory activity during WM encoding upon presentation of a delayed discrimination task that probes load effects in visual WM. Haenschel et al. (2010) subsequently reported that both patients and healthy controls demonstrated an increase in alpha phase-locking with WM load. However, they also reported that patients differed from control subjects, in that they showed generally reduced levels of alpha phase-locking over frontal and occipital electrode sites. In contrast, Bachman et al. (2008) demonstrated that schizophrenia patients and their co-twins displayed a larger increase in ERS magnitude with increasing memory loads, relative to controls. In a recent MEG study, Koh et al. (2011) reported that schizophrenia patients showed diminished alpha event-related desynchronization compared with control subjects upon application of auditory oddball paradigm. Furthermore, these authors also showed that alpha inter-trial phase coherence was lower in the schizophrenia patients than ultra-high risk subjects, and lower in the ultra-high-risk subjects than normal control subjects. Abnormal delta and alpha oscillatory responses in

SZ patients compared to healthy controls were also reported by Ince et al. (2009). Future research is needed to clarify the contradictory results on evoked/event-related alpha responses in working memory paradigms.

Studies comparing schizophrenia patients with healthy controls upon application of a combined TMS- EEG method were begun very recently. Jin et al. (2006) hypothesized that frontal lobe rTMS with individualized stimulus rate at subjects' peak alpha EEG frequency (8–13 Hz) would be most effective as a treatment (alpha TMS). These authors reported that individualized alpha TMS (aTMS) demonstrated a significantly larger therapeutic effect than the other 3 conditions (3 Hz, 20 Hz, sham stimulus). Furthermore, these clinical improvements were found to be correlated with increases in frontal alpha amplitude following aTMS. Accordingly, Jin et al. (2006) concluded that their results affirm that the resonant features of alpha frequency EEG play an important role in the pathophysiology of schizophrenia. Table 1 describes comparatively changes in alpha activity in few diseases.

The dysfunction of cognitive network in AD may be a result of balance disorder between neural excitation and inhibition through neurotransmitters, and disorder of long-term potentiation that strengthens or weakens the synaptic connections (Lisman and Spruston, 2005).

Acetylcholine-containing (Ach) projections from Nucleus basalis Meynert degenerates first in AD (Mesulam et al., 2004). This depletion seems to have a role in dysfunction in visuo-spatial system and memory related tasks in AD. Ach promotes visual-feature detection or signal-to-noise ratios in sensory processing (Hasselmo et al., 2006) and cholinergic medication can improve a normal pattern of task-dependent parietal activation in AD. Working memory tasks (Saykin et al., 2004) or visual search (Hao et al., 2005), visual attention (Balducci et al., 2003) studies indicate an enhancement in prefrontal cortex activity after cholinergic medication, similar to the electrophysiological findings shown by our group

(Yener et al., 2007; Güntekin et al., 2008). An fMRI study in mild AD/MCI also showed a similar pattern in left prefrontal regions during attentional demands (Dannhauser et al., 2005). The diffuse innervation of cortical cholinergic neurones (Sarter et al., 2001) can lead to cholinergic modulation in both higher-level (e.g. fronto-parietal) and lower-level (e.g. visual) areas. It is possible that visual-event-related oscillatory deficits in AD may be related to reduction in cholinergic modulation of visual cortex and attention-related fronto-parietal cortices (Perry and Hodges, 1999).

Understanding how the cholinergic system affects visual sensory or cognitive function is important for Alzheimer's disease. When two types of tasks, i.e. deep minus shallow visual stimulation, were given to AD patients and controls, fMRI showed that the right parietal (Hao et al., 2005), left prefrontal and superomedial prefrontal cortex were less activated by this task effect in AD patients than in controls (Bentley et al., 2008). The extent of involvement of visual and higher-order-association cortex increased with greater complexity in AD. Visual tests were found to activate both primary and secondary visual areas in dorsal stream (Förster et al., 2010). The visual dorsal stream, which involves the parietal lobe, is activated before the ventral stream, which includes the temporal lobe. The parietal lobe is activated within 30 ms after occipital activation, occurring at about 56 ms. Visual sensory areas generally continue to be active for 100–400 ms prior to motor output. The feedback processes between sensory, parietal and prefrontal cortices take about 200 ms for interactive processing. This initial volley of sensory afference through the visual system and involving top-down influences from parietal and frontal regions, occurs much earlier than the early ERP components (Foxe and Simpson, 2002). Using visuospatial paradigms, these regions are particularly sensitive to cholinergic modulation (Sarter et al., 2001). Acetylcholine seems to have a role in promoting visual-feature detection or signal-to-noise ratios in sensory processing (Hasselmo and Giocomo, 2006) and cholinergic medication can promote a normal pattern of task-dependent parietal activation in AD.

Changes in AD subjects on cholinergic medication;

Cortical acetylcholine (Ach) is hypothesized to modulate either the general efficacy of the cortical processing of sensory or associational information or, more specifically, to mediate the subjects' abilities to select stimuli and associations for further processing (Sarter et al., 2005). Basal forebrain is the main source of Ach in the neocortex and Alzheimer patients show depletion of cortical Ach due to degeneration of basal forebrain early in the course of illness (Mesulam et al., 2004). Therefore, cholinergic treatment has been the main treatment option in AD for almost the past 20 years. Increasing cholinergic input can also restore hemodynamics in clinical responders (Claassen and Jansen, 2006). An early study of resting EEG showed that alpha power was reduced following experimental damage to this cholinergic pathway (Holschneider et al., 1998). In addition to basal forebrain, glutamatergic and cholinergic mechanisms within the prefrontal cortex may also regulate Ach release in other regions, such as the posterior parietal cortex (Nelson et al., 2005). The ability of prefrontal cortex to regulate transmission in more posterior cortical regions may represent a “top–down” mechanism to control attention (Sarter et al., 2005). For example, thalamocortical fibers are suppressed much less than intracortical connections by acetylcholine, thus possibly enabling the afferent input to have a relative effect in the cortex (Kimura et al., 1999). Therefore, the detrimental performance effects of an ongoing distracter are diminished, most likely by increasing the cholinergic processing of sensory inputs (Sarter et al., 2005). These agents can improve the latencies of the visual P300 in AD patients (Reeves et al., 1999). Earlier functional imaging studies showed that, after administration of AChEI, clinical responders to treatment selectively displayed improvements over left cingulate and prefrontal-parietal areas (Potkin et al., 2001; Vennerica et al., 2002; Nobili et al., 2002; Mega et al., 2005).

4. REASONINGS AND SUGGESTIONS FOR UNDERSTANDING INTEGRATIVE FUNCTIONING OF ALPHAS

As a consequence of the results surveyed in the present review, a chain of “Reasonings and Suggestions”, based on empirical evidence, will be outlined in the following section:

4.1. Multiple Functional Correlates of Alpha Activity

(1) *Alphas have multifold functional correlates*. 10-Hz rhythms have important functional correlates, including sensory, motor and memory functions. Alpha oscillations serve as building blocks in several functions.

(a) Different 10 Hz oscillations (alphas) can be recorded from various areas of the human scalp and intracranial structures of the cat brain. They are related to diverse sensory and/or cognitive functions, and are also topology-dependent.

A unique functional correlate cannot be assigned to alpha activity.

Since the work of Adrian, "evoked alpha" was regarded as a sign of the reactiveness of the CNS to sensory stimuli. Sensory-evoked 10-Hz responses were recorded in several cortical and intracortical structures.

Sensory stimulation can also evoke 10-Hz oscillatory behavior at the cellular level (Creutzfeldt et al., 1966; Dinse et al., 1997; Lopes da Silva, 1993) and *“Evoked 10-Hz oscillations”* can be selectively generated in several structures of the brain simultaneously. The dampened oscillations (of approximately 200–300 ms duration) after sensory stimulation are sensitive to the modality of stimulation and the recording site. When subjects are loaded with a cognitive task, *event-related alpha rhythms* are generally prolonged.

(b) Alpha and motor processes: The results of Pfurtscheller et al. (1996) on motor correlates of alpha activity were explained in detail. At this point, we should again mention the statements of Llinàs (1988), who assigned diverse functional roles to oscillations and resonances in the central nervous system.

(2) *Alpha as a universal code or universal operator.* The results mentioned above underline the major physiological meaning of 10-Hz oscillations, which may be comparable to the putative universal role of gamma responses in brain signaling.

(3) As a consequence of the present survey, describing multiple general processes and *multifold functions* according to sensory-cognitive modality and topological differentiation, actual hypotheses on alpha activity can be discussed with the following steps:

> a) A critical evaluation shows that most working hypotheses result from observation of partial data and resulting statements are therefore of limited applicability; alternatively, one may talk about limited or interim hypotheses.
>
> b) It seems plausible to propose that such interim hypotheses should comprehend (encompass) multiplicities consisting of several topologically-distributed neural oscillations and neural/functional processes.
>
> This means: Not only alpha oscillations but multiple oscillations within the whole cortex must be taken into consideration, reflecting *Alpha's* role in numerous functional processes. Vice versa, almost all functional processes (sensory + cognitive) are manifested by several oscillatory components besides alpha.
>
> c) The description of alpha activity in the whole cortex by means of stack plots (Figure 2) is fundamental before considering new theories. Namely, alpha responsiveness is also a function of spontaneous activity.

(4) An ensemble of parameters as *spontaneous alpha, event related alpha responses and coherences* may, in future, be used as clinical biomarkers of cognitive impairment in schizophrenia, Alzheimer's disease and bipolar disorders. In turn, results related to the attenuation or absence of alpha activity in clinical studies may be useful for topological component analysis of cognitive functions as working memory, perception and learning deficits.

(5) Emotion and functions, related to emotional events, play a considerable role in integrative brain function, as described by Le Doux (1999) and Solms and Turnbull (2002), in Section 2. Emotional inputs considerably influence event-related alpha responses.

(6) In order to achieve a profound functional analysis by means of oscillations, it is suggested to work (where possible) with a broad strategy, including sensory and cognitive stimulations. Measurements with only cognitive load prior to determining the sensory components may lead to restricted interpretations. All memory processes are interwoven with *phyletic* memory and *perception* (Fuster, 1995, 1997; Goldman-Rakic, 1996, etc.). This suggestion is also most important for the analysis of ERD.

(7) The strategy of analyzing *evoked/event-related coherences* is not yet broadly applied. Coherences manifest coherent activity of sensory and cognitive networks, *triggered by a sensory or cognitive task*. Accordingly, cognitive response coherences comprehend activation of a greater number of neural networks that are, most possibly, not activated, or less activated, in the EEG and sensory evoked coherences (Figures 15, 16). Not only thalamo-cortical circuits, but also the role of reticular formation must be considered in all function-modeling purposes.

8) The role of alpha activity in cognitive processes merits considerable attention. It is inevitable to introduce standardization related to frequency compositions, and; amplitudes and topological dependence of alpha in childhood and the maturing brain (see Section 7). If such standardization cannot be introduced, all efforts to measure memory performance in elderly subjects and cognitively impaired patients will be restricted.

9) If lesions, atrophy or volumetric changes are detected, a change of alpha activity can also serve as component analyses (see the work by Babiloni et al., 2009a), indicating decreased alpha in accordance with volume changes in hippocampus (Section 2).

5. CONCLUDING REMARKS AND SHORT SYNOPSIS

The brain is the most complex system in the known universe and, in both reviews, we presented empirical evidence related to the dynamics of the brain, i.e. a biological system that is continuously changing. Assuming that the brain is an organ, which also controls our mind and our body, the understanding of brain dynamics should help in the search for the communicative processes between the body and the brain. In addition to electrical oscillations, the brain–body machineries are also controlled by the release of neurotransmitters. Furthermore, the oscillatory activities in the brain and body are affected by these transmitters; the electrical processes also control the release of transmitters.

Questions such as "*what is the mind*?" and "*what is the brain–body–mind?*" can be approached only by functional and comparative analysis of the *ensemble of brains*, and links that are shown in Figure 3. The schematic in the upper part of Figure 3 shows that the machinery of brain–mind cannot be understood only by analyzing processes at the level of the adult human brain. Our thesis is this: In order to approach the brain–mind, we also have to observe the machineries of invertebrate ganglia and brains during the evolution of species. Furthermore, physiological processes and anatomical changes need to be analyzed during maturation of the brain, from infancy through adulthood, to old age. (Companion reports Section 7)

In pathologic brains, the release of transmitters and, accordingly, oscillatory processes and control of cognitive processes, are highly altered (see Section 3). Therefore, the analysis steps in Figure 3 include a loop indicating the influences of pathology (Alzheimer, Schizophrenia, Bipolar Disorders) that constitute a minimal analysis-prerequisite to approach the integration of brain–body–mind (Başar et al., 2012a).

When we go through several parts of both present reviews and learn about sensory-cognitive processes, electrophysiology in evolution of species, differences between child and adult brains, memory activation and emotional brain, we observe results indicating that oscillatory processes and transmitters are interwoven with all types of processes in brain–body integration. The available empirical evidence leads us to describe the concept of "*quasi-invariants*" as building blocks in brain–body integration.

1) Moreover, in the adult brain, 10-Hz oscillations depend on the related function and topology: For example, the occipital cortex shows high amplitude, regular alpha activity, whereas the frontal cortex has poor alpha activity during resting conditions. Upon increase of cognitive load, 10-Hz oscillations are also observed in the frontal cortex. In Alzheimer's patients, alpha is reduced, and is almost completely absent in bipolar disorder.

2) Several examples show that alpha oscillations are not present at the same area during application of different task conditions to the brain. By observation of responses to various facial stimulations (*angry face*, *happy face*), i.e. during emotional processes, the activated oscillations are altered by observation of angry faces: occipital beta response increases during observation of angry faces, and occipital alpha activity is also increased.

3) Is the mind of a child different from the adult? Is the mind of an Alzheimer patient different from a healthy subject of the same age? There are crucial differences between the oscillatory patterns of healthy and Alzheimer subjects, and of bipolar subjects (Section 3).

According to the factors explained above, we simply state that alpha oscillatory responses are the building blocks of dynamic processes and, because of the crucial changes in amplitude, location and dependence on modality, age and disease, we describe them as *quasi-invariants* in brain–body–mind integration.

4) We must also note that, not only the parameters of oscillatory patterns but the *selective connectivity of alpha oscillations* between various structures of the brain, is vital for

brain functioning when studying coherences in the healthy adult brain and in clinical disorders (Section 3).

When we take into consideration all of the results, models and hypotheses in the present reviews, at first glance, one can state that a reliable theory of alpha is extremely difficult. Instead, we propose that it would be more reasonable to collect highlights, results and exclusion principles from the results, with the aim of excluding somewhat controversial trends, at least in order to avoid errors.

The brain does not respond in a homogenous, standard manner with invariant response amplitudes; the responses are highly dependent on topology, age, states and pathology. The alpha activity, alpha responses and coherences are selectively distributed. Accordingly, it is suggested that new, reliable hypotheses should be pronounced only after performing or surveying a wide spectrum of measurements described in the schematic flow chart.

The observation of pathological changes in alpha activity opens the way for a more reliable understanding of functional correlates of alpha in brain function. This is the only way in which to discover the *web of oscillations and neurotransmitters*. Further, the results upon the application of neurotransmitter-based drugs can help to clarify the basic role of neurotransmitters in modification of oscillations. Thus, the analysis of alpha activity in cognitive impairment may also help greatly in understanding brain processes in healthy subjects.

In the 1960s, alpha activity and EEG was considered as “smoke” or idling of the brain, and was neglected by most neuroscientists (See the remark by Ross Adey in the companion review, Section 1). Significant subsequent developments in our understanding mean that alpha is now regarded as a most important signal in the understanding of cognitive processes. However, the reasonings outlined above show that it would also be a mistake to consider “alphas” as a sign of limited cognitive events. Alpha oscillations are among the most important building blocks for functioning, association and communication in the whole brain and body.

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LEGENDS:

Figure 1: Structure of memory (Modified from Atkinson and Shiffrin, 1968).

Figure 2A: Power spectra and mapping analysis of spontaneous alpha activity in healthy subjects and in euthymic bipolar patients. Note the greatly reduced alpha in euthymic patients (Modified from Başar et al., 2012b).

Figure 2B: Power spectra and mapping analysis of evoked alpha activity in healthy subjects and in euthymic bipolar patients. Note the greatly reduced alpha response in euthymic patients (Modified from Başar et al., 2012b).

Figure 3: Schematic explanation of proposed analysis steps for an approach to brain–body–mind. The expression “body” refers to ensembles of oscillatory processes in the vegetative system, particularly in the cardiovascular system. (Modified from Başar 2011)

Figure 4: Schematic differentiation of Brain’s Alpha Oscillations

Table 1: Pathological changes in alpha response

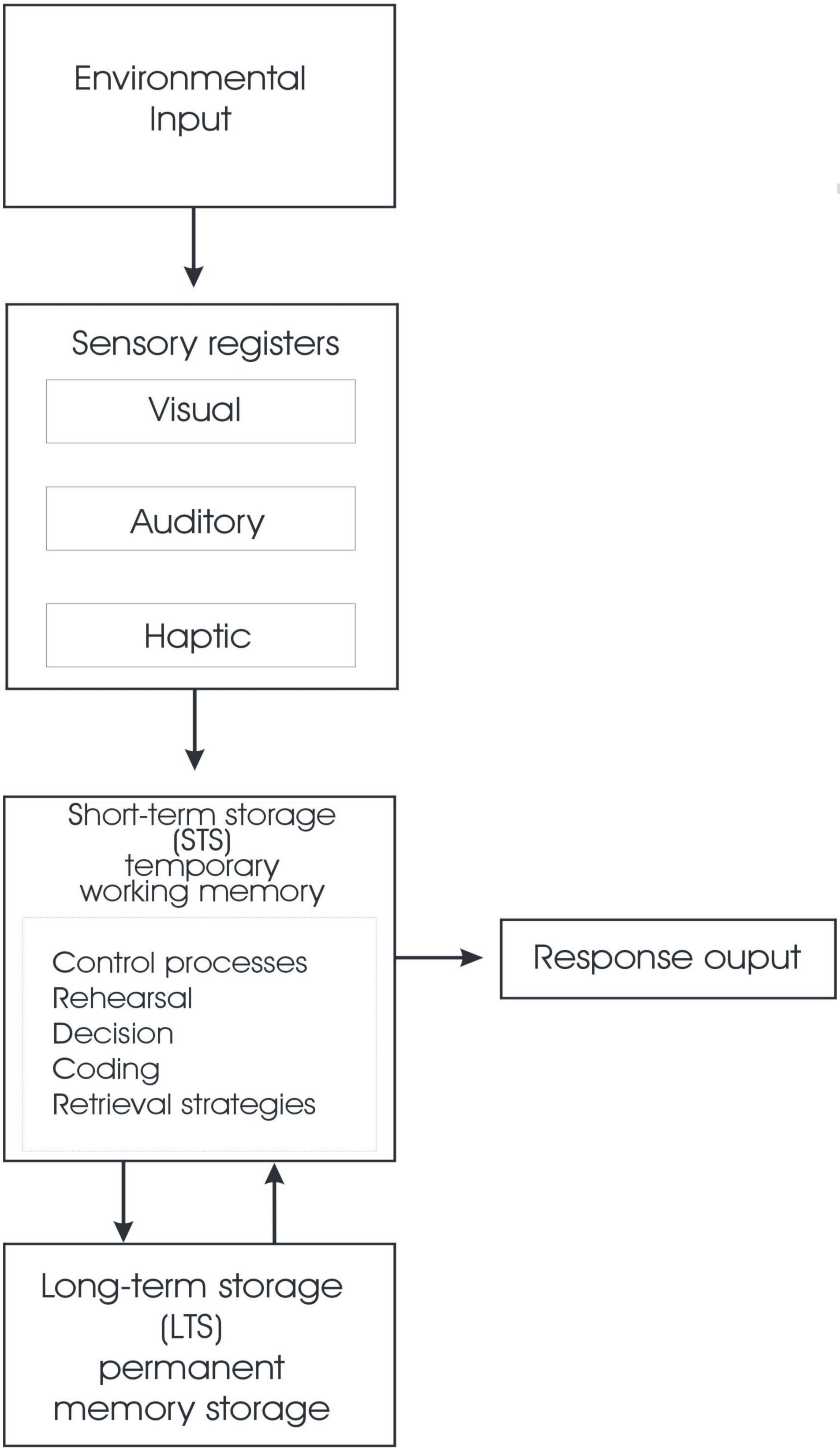
Environmental
Input
Sensory registers
Visual
Auditory
Haptic
Short-term storage
(STS)
temporary
working memory
Control processes
Rehearsal
Decision
Coding
Retrieval strategies
Response ouput
Long-term storage
(LTS)
permanent
memory storage

Figure 1

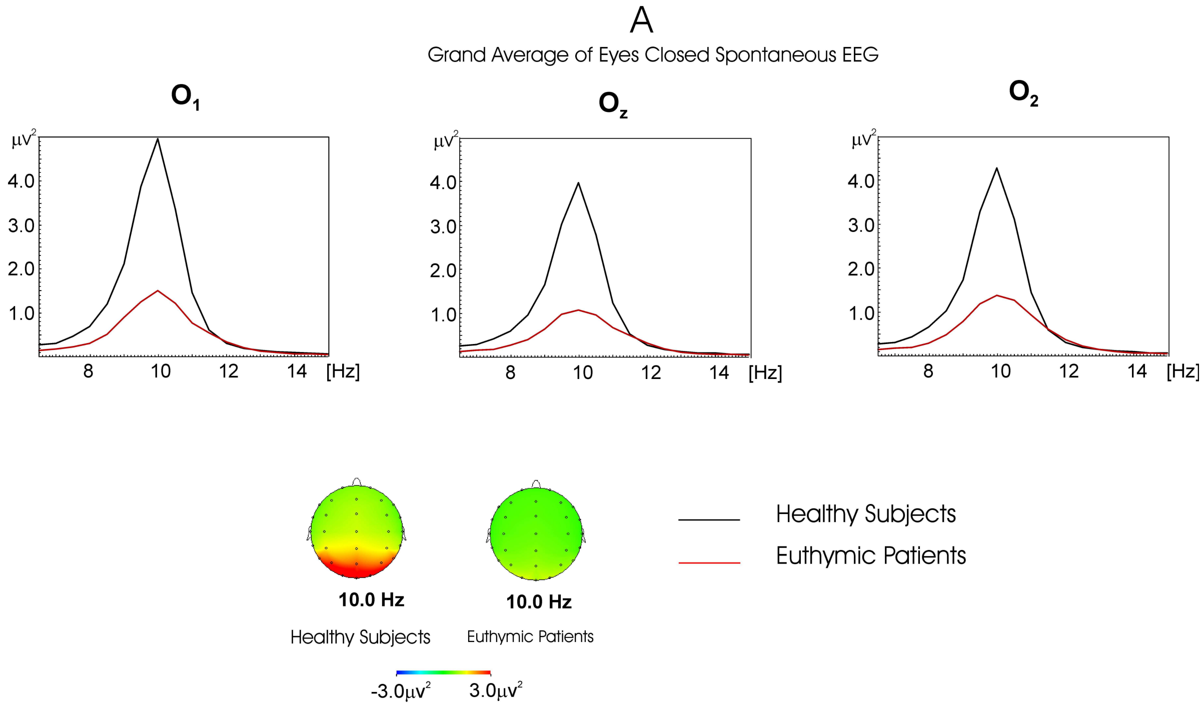
A
Grand Average of Eyes Closed Spontaneous EEG
O_1
O_z
O_2
μV^2
4.0
3.0
2.0
1.0
8
10
12
14
[Hz]
10.0 Hz
Healthy Subjects
10.0 Hz
Euthymic Patients
-3.0μv^2
3.0μv^2
Healthy Subjects
Euthymic Patients

Figure 2A

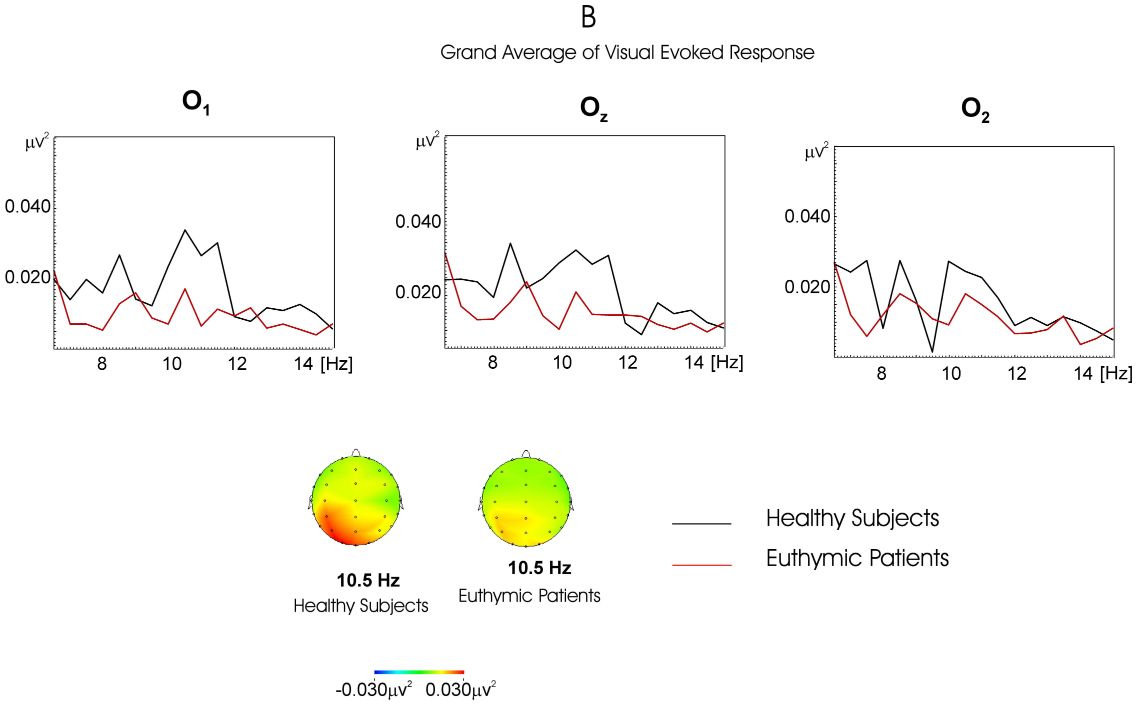
B
Grand Average of Visual Evoked Response
O1
Oz
O2
μV2
0.040
0.020
8
10
12
14 [Hz]
10.5 Hz
Healthy Subjects
10.5 Hz
Euthymic Patients
Healthy Subjects
Euthymic Patients
-0.030μv2
0.030μv2

Figure 2B

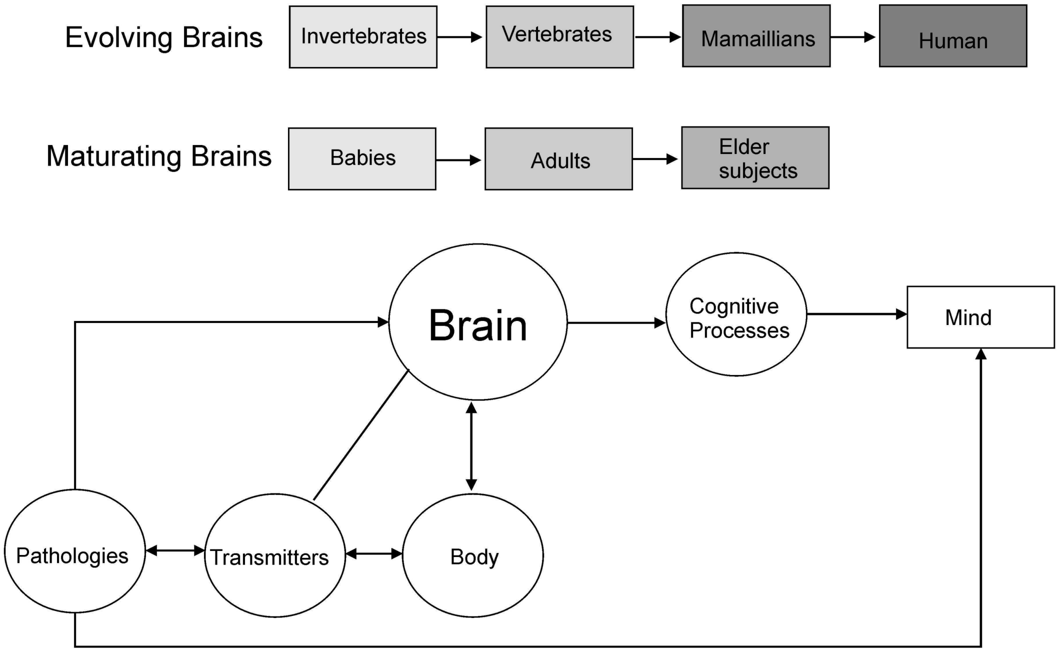
Evolving Brains
Invertebrates
Vertebrates
Mamaillians
Human
Maturating Brains
Babies
Adults
Elder subjects
Brain
Cognitive Processes
Mind
Pathologies
Transmitters
Body

Figure 3

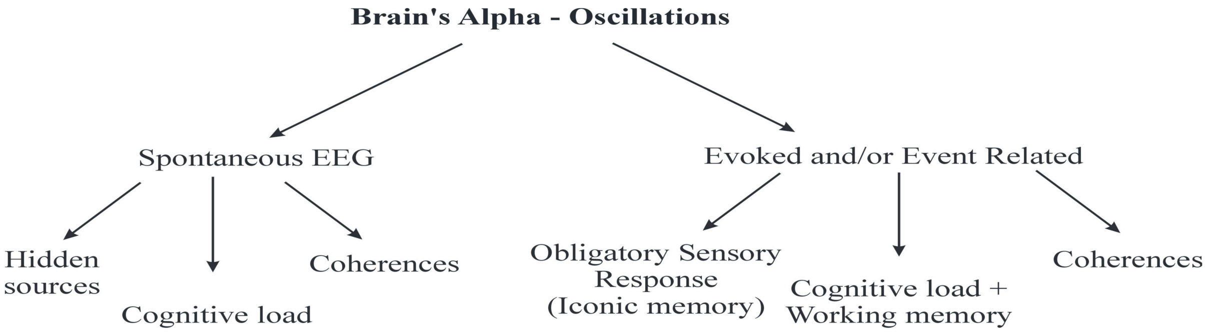
Brain's Alpha - Oscillations
Spontaneous EEG
Evoked and/or Event Related
Hidden sources
Cognitive load
Coherences
Obligatory Sensory Response (Iconic memory)
Cognitive load + Working memory
Coherences

Figure 4

Table 1

	Pathology	**Modality and Paradigms**	**Methods**	**Results**
Kikuchi et al., 2002	Alzheimer's Disease.	White flickers at 5, 10 and 15 flashes/ sec.	Evoked coherence.	AD patients had significantly smaller coherence than healthy elderly subjects in the 2nd (10 Hz) and 4th (20 Hz) harmonic responses to 5 Hz.
Hogan et al., 2003	Alzheimer's Disease.	Memory paradigm.	Evoked power; Evoked coherence.	Normal controls but not AD patients respond to memory demands by increasing upper alpha power over temporal cortex. Reduced alpha evoked coherence in patients.
Babiloni et al., 2005	Alzheimer's Disease (AD) and 10 vascular dementia (VaD).	Visual delayed choice reaction time tasks.	ERD/ERS MEG study.	Alpha ERD showed greater peak amplitude in demented patients than in normal subjects.
Zeng-Yan, 2005	Alzheimer's Disease.	Photic Stimulation.	Evoked coherence.	Reduced alpha evoked coherence.
Güntekin et al., 2008	Alzheimer's Disease.	Visual oddball.	Event-related coherence.	Reduced alpha evoked coherence in unmedicated Alzheimer patients; medicated (cholinesterase inhibitors (AChEI) patients have similar evoked alpha response to healthy controls.
Başar et al.,	Alzheimer's	Visual oddball.	Event-related	Reduced alpha evoked

2010	Disease.		coherence.	coherence in unmedicated Alzheimer patients.
Özerdem et al., 2008	Bipolar Manic.	Visual oddball.	Peak-to-peak amplitudes of averaged alpha responses.	Lower alpha response in bipolar manic patients.
Başar et al., 2012b	Bipolar drug-free euthymic patients.	Basic visual signal.	Evoked alpha power.	Reduced evoked alpha power in bipolar disorder patients.
Pin-Shiuan Lee et al., 2010	Bipolar Disorder (BD) and Major Depressive Disorder (MDD).	Emotional task with facial image stimuli.	Time–frequency analysis MEG study.	Alpha-beta rhythm increases in BD patients.
Rice et al., 1989; Jin et al. 1990, 1995, 1997, 2000; Wada et al., 1995	Schizophrenia.	Periodic photic stimuli, visual steady state.	Evoked power.	Schizophrenia patients exhibited reduced power in the alpha frequency range compared to healthy controls.
Bachman et al., 2008	Schizophrenia.	Match to sample task.	ERD/ERS.	Schizophrenia patients and their co-twins showed a greater increase in ERS magnitude with increasing memory loads, relative to controls.
Başar-Eroğlu et al., 2008	Schizophrenia.	Visual oddball.	Evoked power and phase locking.	Neither amplitude enhancement after stimulus onset nor intertribal coherence was generally reduced in patients. Healthy controls elicited maximum early alpha and late theta response over occipital electrode sites, while the maximum response in

				patients was shifted to anterior electrode locations.
Brockhaus-Dumke et al., 2008	Schizophrenia.	Auditory paired-click paradigm.	Phase-locking analyses, single trial amplitudes	Phase-locking of the alpha frequency band was significantly reduced in patients.
Başar-Eroğlu et al., 2009	Schizophrenia.	Auditory continuous performance task.	Peak-to-peak amplitudes of averaged and single-trial data.	Amplitudes from patients were reduced at F_z and C_z locations only for the early time window (0–250 ms) upon non-target stimuli.
Ramos-Loyo et al., 2009	Schizophrenia.	Three oddball paradigm tasks, (face and facial expression).	Peak-to-peak amplitudes of averaged data, Root Mean square (RMS).	Grand-averaged alpha oscillations demonstrated higher RMS values in the occipital leads in schizophrenia compared to controls and the opposite over frontal regions.
Haenschel et al., 2010	Schizophrenia.	Delayed discrimination task.	Phase-locking.	Alpha phase-locking increased with working memory (WM) load in both SZ and control subjects. Alpha phase locking was generally reduced in SZ compared to healthy controls.
White et al., 2010	Schizophrenia.	Vibrotactile somatosensory task.	EEG-fMRI Evoked power.	In healthy individuals, the strongest component was dominated by alpha oscillations, and was associated with activity in somatosensory regions, the insula, anterior cingulate cortex. In schizophrenia, the strongest component had low alpha power and activity was limited mainly to somatosensory regions.

Highlights

► The short review describes alpha activation in cognitive processes and cognitive impairment. ► Changes of alpha activity in processes of emotion and memory are described. ► It also outlines reasoning for understanding of alpha in integrative brain functions.