A Proposal to Extend Brodmann's Areas Concept to a New Model

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ABSTRACT

Since the beginning of the last century, the localization of brain function is presented by Brodmann areas, or maps that are a result of anatomic organization. They are used in order to give a global idea of cortical structures for given sensory cognitive functions. In the last decades, the analysis of brain oscillations gained high importance for the correlation of brain functions. Moreover, the use of the spectral connectivity provides information on dynamic connectivity between various structures. Beside this, according to (Luria, 1966), brain responses have dynamic features and structural localization is almost impossible. According to these uses, brain functions are very difficult to localize and need joint analysis of oscillation and event related coherences. In the present report, a model called "CLAIR" is described to extend and possibly to replace the concept of the Brodmann areas. To design a perfect functioning CLAIR model requires years; however, the beginning step is provided in the present report.

Key Words: Brodmann, EEG, Oscillations, Functional Map, CLAIR

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1. Introduction

One of the most important steps to understand brain function was performed by German neuroanatomist Korbinien Brodmann at the turn of 20th century. The areas of Brodmann were based on cytological neural organization, and the boundaries of the Brodmann areas were based on histologic examination. Since the idea of Brodmann areas were derived from the neuron doctrine of Ramón y Cajal, it seems important to consider another important discovery: The Electroencephalography by Hans Berger. The neuron doctrine presents the idea that single neurons are responsible and sufficient for performing brain functions. The brain is not a "syncytium" as the neuron doctrine says. On the contrary, EEG activity, which is also, called brain oscillations; do reflect activity of neuron populations.

Although in the 1970's, the EEG signals discovered by H. Berger in the 1930's were considered as "noise" or "smoke of the brain," at the end of the 20th century, several measurements have demonstrated that brain oscillations belong to the most important building blocks of brain functions (Başar, 1980; Buzsaki, 2008; Başar, 2011). Moreover, studies of long distance event related coherences have shown that single areas of the brain cannot be correlated with different brain functions. Instead, upon stimulation of the brain with sensory and cognitive signals, the activation in adequate areas of the brain triggers different oscillatory activities; and the connectivity (the spectral connectivity, special coherences) changes considerably upon stimulation modality and recording sides.

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These findings have a crucial consequence; Brodmann areas are not sufficient to describe the topological dynamic organization of brain function. The whole brain work or whole cortex organization is much more complicated than the description of the Brodmann areas. Another important fundamental idea is expressed in Luria's statement.

According to (Luria, 1966) there are no anatomical centers for the psychological functions of the mind. Mental functions, too, are the products of complex systems, the component parts of which may be distributed throughout the structures of the brain. The task of neuroscience is therefore not to localize the "centers," but, rather, to identify the components of the "various complex systems" that interact to generate the mental functions. Luria called this task "dynamic localization." Mental functions, in short, are not localized in any of the component structures, but rather between them. Like the mental apparatus as a whole, they are virtual entities (Solms and Turnbull, 2002).

According to the present results, the understanding of whole brain function also requires the analysis of spectral coherences, i.e., the increased connectivity between structures upon cognitive load, together with enhanced temporal oscillatory responses. Furthermore, in addition to Luria's view, it seems that Brodmann's (1909) areas should be extended to a more dynamic presentation, in which sensory and cognitive areas should be described as superposition of multiple primary and secondary functions.

As a consequence of the above concluding remarks, and especially the views of Luria and the concept of dynamically linked Brodmann's areas, we propose that all sensory-cognitive paradigms (as is here the case in P300-oddball) must be jointly analyzed in terms of oscillatory responses and related coherences. Only in this way, is it possible to open new avenues for description of whole cortex organization. This description will be achieved by the CLAIR model.

2. Interim summary of emphasized concepts

According to the facts described in previous section, we tentatively assume that functional mapping of the brain has to be presented with the concepts of the dynamic functional areas. In order to achieve such functional mapping, we have to take into account several new measurements and concepts:

- Superposition of the oscillations (alpha, beta, gamma, delta, theta) (Başar, 1980)
- The Luria's concept (1966)
- Coherence in space (spatial connectivity)
- Coherence in time (phase-locking)
- Differentiation of sensory and cognitive tasks with simple and cognitive stimulation.

Change of the above results in diseases and following drug application.

3. Newer trends to present the brain function with neural populations

When the brain performs sensory-cognitive processing, the degree of activations in different areas of the cortex are continuously modified according to the Luria's concept and all type of event related oscillation results as described by (Başar, 2011). Primary sensory cortex, all type of association cortices, parietal lobes, and the limbic system, are in a reverberating process. In other words, in the finalization of complete functions, the activation of the neural group do perpetually change. The result is similar to the performance of a giant neuron group, which is composed of several sub-populations. For example, in the attention process the volume and shape of these complex neural groups do change. In comparison to the evaluation of simple sensory signals, in the 1980's Roy John proposed a module, which is responsible for the activation of a given brain function: "the hyperneuron." However, Roy John did not describe a dynamic construct including connectivity between neural populations. Similar to Roy John, (Fuster, 2013) launched the idea of cognits that are unitarily cognitive elements responsible for the organization of brain functions. According to Fuster, cognitive information is acquired and stored in a web of distributed, intermeshed, and overlapping networks. He named these units as "*cognits*" that are units of knowledge. They are formed by life experience in the cortex of association and foundation of phyletic memory. Life experience generates those networks of cognits, which constitute structure patterns of association between neurons representing more elementary aspects of perceptions and actions. This richness of cortices is not present in given

locations; they are structures of neurons or ensembles in order to store information much like a new computer. On the contrary, this richness builds cognitive codes.

At this point, we start to describe the philosophy of the CLAIR-Model, which is essentially similar to the hyperneuron and also to extended cognits. In our new model CLAIR, we attribute to several areas of the cortex several oscillatory networks to generate EEG oscillations as alpha, beta, gamma, theta, and delta oscillations. Furthermore, we also add an important building block for connections of the long distance areas of the brain. This is spectral connectivity, which is measured by coherence functions. Neural populations that are activated by sensory cognitive stimulations are linked and measured with coherence functions. A CLAIR module presents the assembly of neural populations, which rise to the integration of functions. Depending on the complexity of the signals, this module can be smaller or larger; connectiveness can be strong or weak, and the number of activated EEG oscillations and their locations can be extremely difficult to localize. The CLAIR acronym is an abbreviation of the following words: cortical, links, association, integrating, and responsive-areas.

4. How can the preparation of the CLAIR model be realized?

We will present in this report two examples for the design of CLAIR model. For this task we will as a first step illustrate the functional map related to a simple light signal, which triggers evoked oscillations in the brain. In the second step, we will also use light stimulations in order to registrate the response to a cognitive task. This is performed by using the oddball paradigm to record the brain response upon the task of incorporating "perception and decision making, learning, and working memory." We used two different visual signals with slightly different illumination values. One of these light signals was applied frequently; the other light signal was applied infrequently at a random ratio of 20%. The subject has to focus his attention to the infrequent signal, which was defined as the target. Additionally, the subject has the task of mentally counting the occurrence of the "target". This means, light evoked oscillations and event related oscillations provide different responses (Başar *et al.,* 2011; Polich and Koch, 1995).

We know that in both responses alpha, beta, gamma, delta, and theta responses are present; however, the oscillation amplitudes and the positions along the time scale are different. Alpha responses have similar amplitudes in event related oscillations and visual evoked oscillations, but there are prolonged delta responses in the event related oscillations, which are delayed along the time-axis, or it has a second component in the time window around 300 ms after the stimulations. The most important change is detected in the delta response, which is usually triggered in the first 100 ms in the evoked oscillations and event related oscillations. Moreover, 300 ms later, the target delta response is delayed and has a very large component in the time window between 300-400 ms following presentation of the target stimulation.

We now consider the gamma band. Our recent analyses have shown that there are at least three response components upon the target stimulation in the event related oscillations. These responses occurred around 100-200 ms, 400 ms, and 800 ms. These response components also have different response frequencies. For simple light stimulations, these responses usually do not show strong phase-locking components in the late time window. In the target response, phase-locked components are more significant and appeared as phase-locked responses in intertrial coherence plots (Figure 1a and 1b). Certainly, as it was earlier stated, signal processing upon target stimulations is richer in information since the number of neural structures involved in this cognitive processing is higher.

One of the other features in the neural oscillatory organization is "connectivity" between various areas of the brain. The connectivity, or strengths of the links between various structures of the brain, can be measured by means of spatial coherence. There are varied degrees of coherences between functional structures of the brain. As (Figure 3a and 3b) show, simple sensory evoked coherences are not as high as event related oscillatory coherences.

Figure 1a

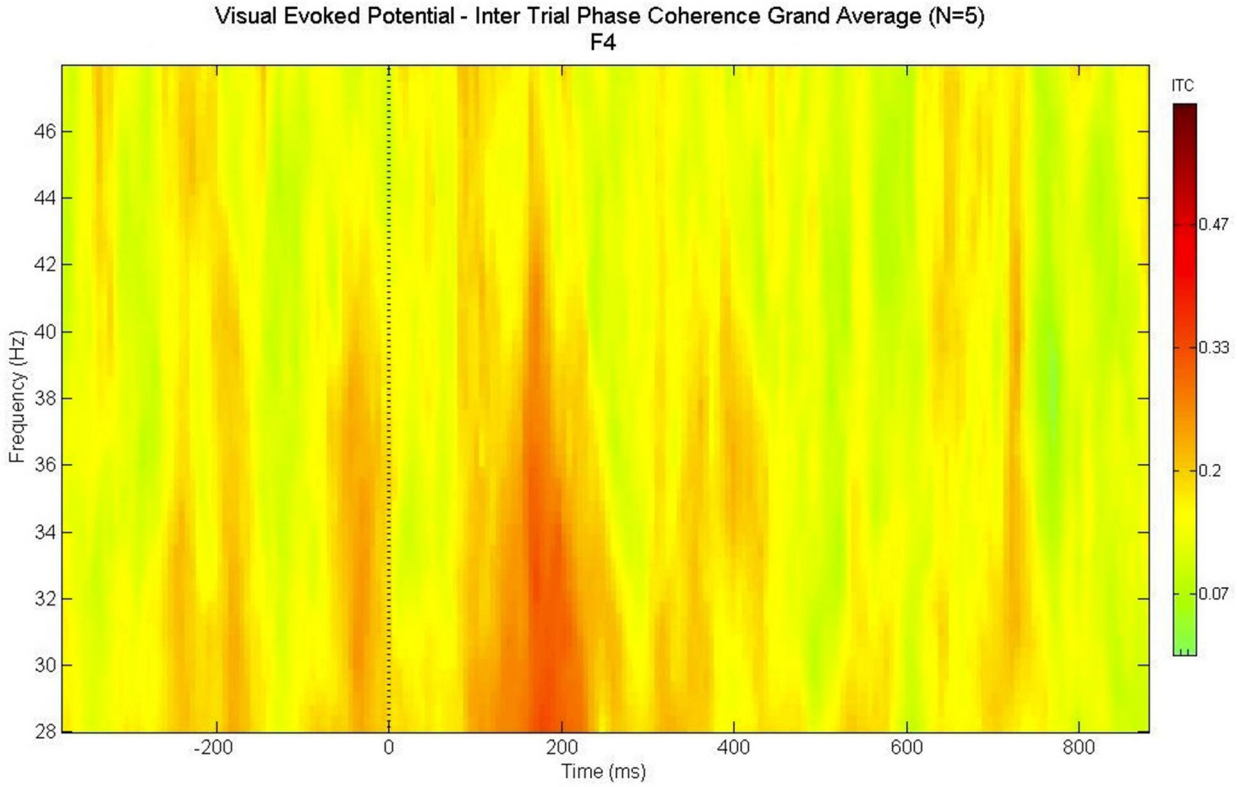

Figure 1b

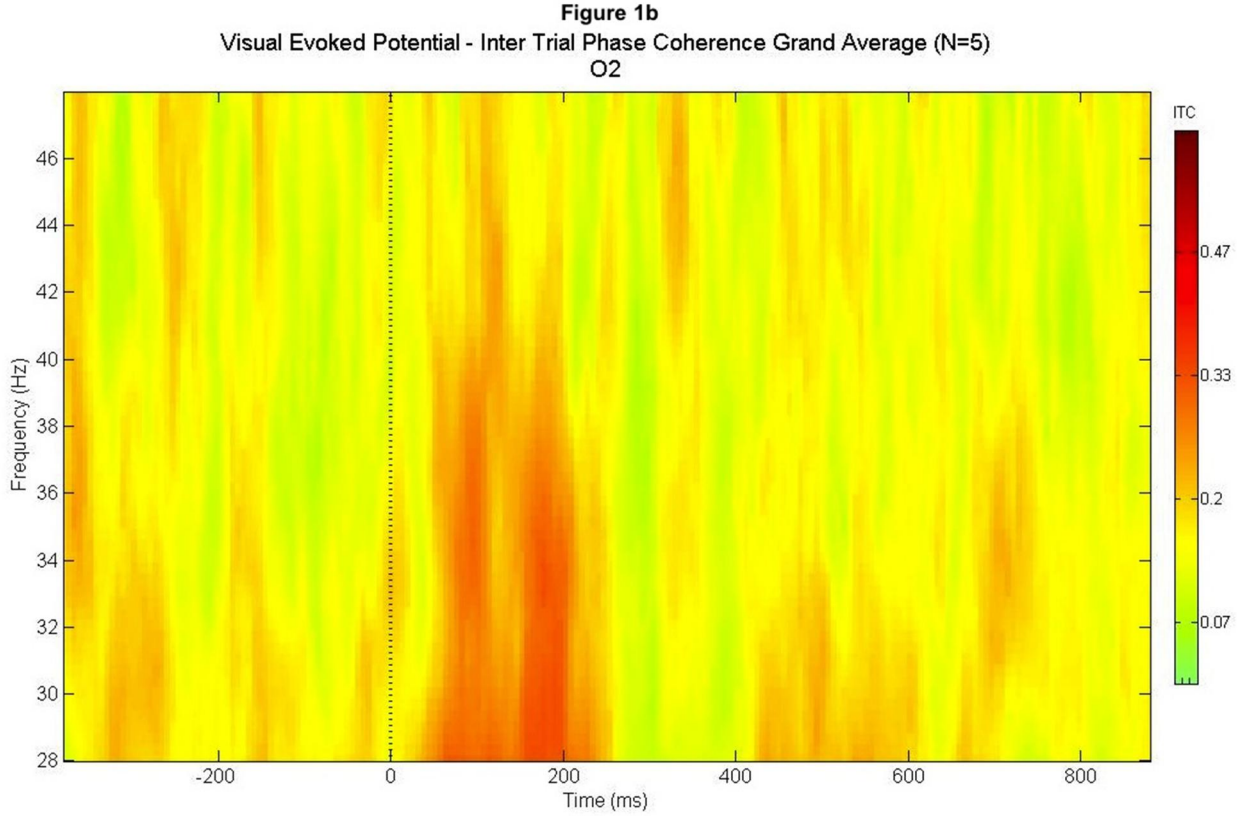

Figure 1a and 1b. The grand average plots of intertrial phase coherence upon simple visual stimulation as grand average of 5 subjects. Modified from Başar, 2012.

Figure 2a

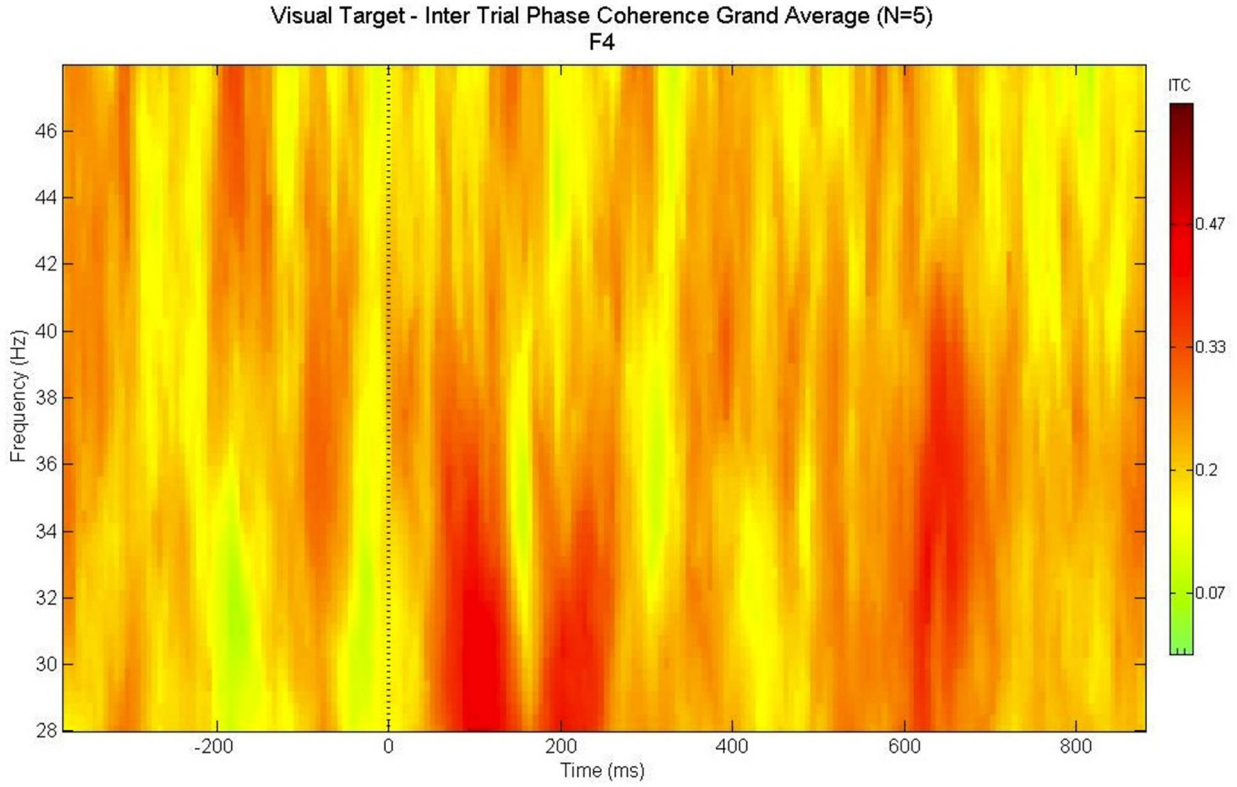

Figure 2b

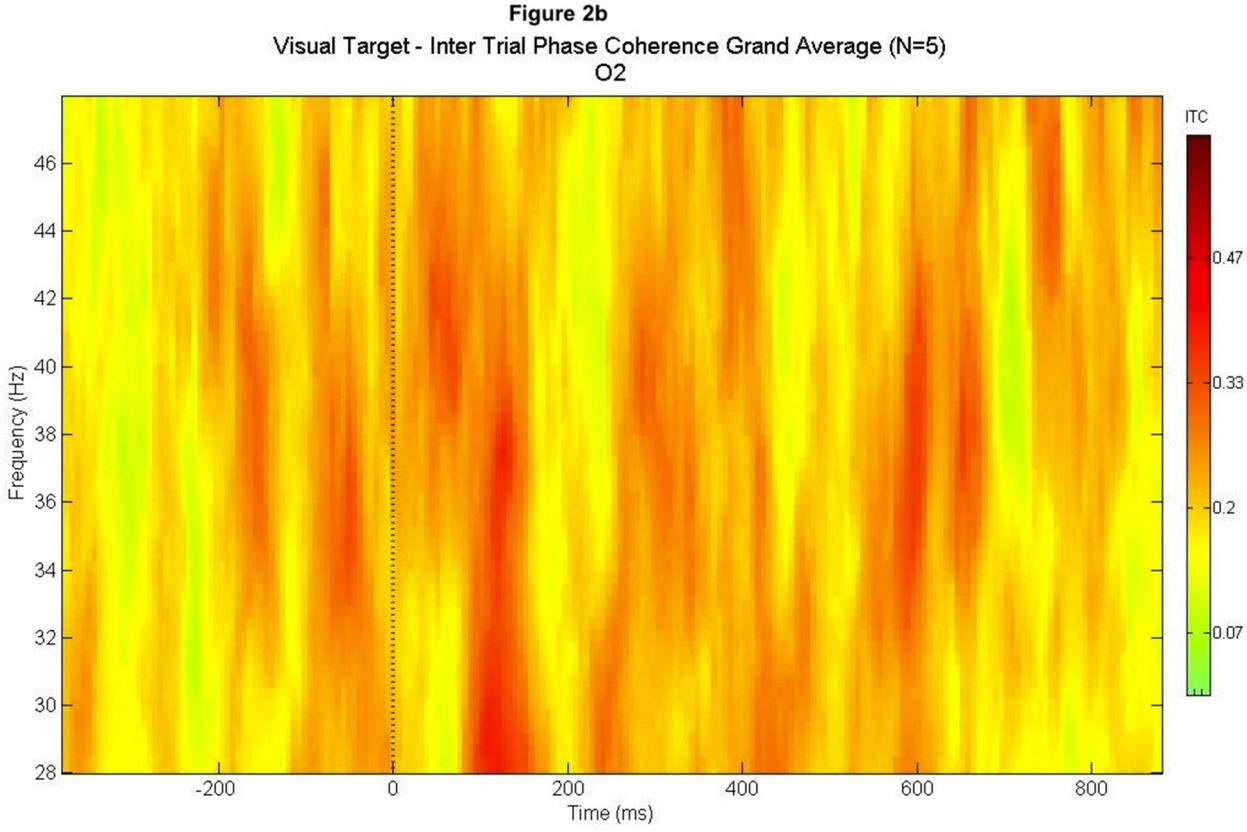

Figure 2a and 2b. The grand average plots of intertrial phase coherence upon cognitive target stimulation as grand average of 5 subjects. Modified from Başar, 2012. Figure 2a and 2b show the intertrial coherence upon presentation of target stimulation for F4 and O2 locations.

The mapping illustration as a result of pure sensory processing and cognitive processes are completely different. In the following sections, we will describe the so-called CLAIR maps that are a result of long standing basic experimental measurements.

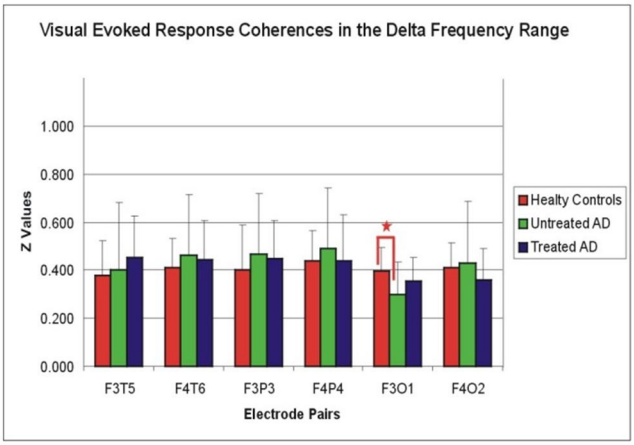

Figure 3a. Mean Z values of healthy controls, treated AD and untreated AD subjects for delta frequency range upon simple light stimuli. "*" sign represents p<0.01. Modified from Başar *et al.,* 2012.

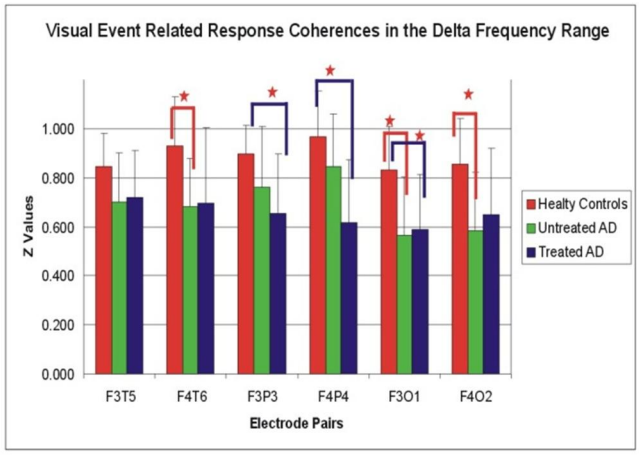

Figure 3b. Mean Z values of healthy controls, treated AD and untreated AD subjects for delta frequency range upon target stimuli. "*" sign represents p<0.01. Modified from Başar *et al.,* 2012.

5. A progressed description of the CLAIR Model

In the meantime, there are many studies about the analyses of P-300 oddball event related potential in the frequency domain. The results are published in several articles and books (Karakaş *et al.,* 2000). When we compare (Figure 4a and Figure 4b), it is immediately clear that in these locations, delta responses are considerably increased due to the application of a visual memory task. The gamma responses are also increased, especially in the frontal and late locations at the time scale. We observed two different theta and delta windows. We merely talk about the "prolongation of oscillations" or "late second window" (a huge oscillatory response in the time domain at around 400 ms). The spatial connectivity upon a cognitive task is increased in alpha, theta, and delta oscillations. Upon simple light, the connectivity between alpha, theta, and delta oscillations are weaker. Z<0.5. This means, the coherence upon application of cognitive task is much higher than the stimulation upon simple visual stimulation.

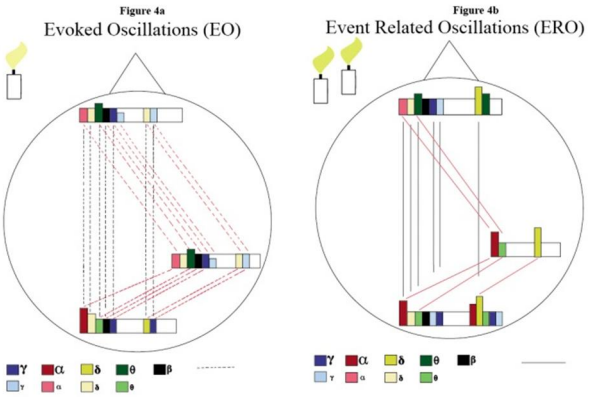

Figure 4a and 4b. The presentation of CLAIR areas upon stimulation with simple light and stimulation of visual target signals. In this illustration, the colored areas represent different oscillations from alpha to gamma. Here only three locations are presented: F4, P4, 0Z.

The colored areas are also differentiated. For example, dark red areas mean higher amplitudes of alpha response; light reds mean low amplitude of alpha. Delta frequency is presented with dark and light yellow. The sequence of the colored locations depends on the time position of stimulations. The time scale for this preliminary presentation is only roughly presented.

The illustration also globally presents the connectivity between various structures. Dashed lines are correlated with lower coherences (Z<0.5). Thick lines are correlated with higher coherences up to Z=1. The knowledge of the existence of lower and higher coherences is derived from (Figure 3a and 3b). In these illustrations, we present only three areas at the right side. It is planned to design CLAIR maps with at least 15 electrodes, and to show exact time positions, and exact cortical

locations. This type of CLAIR maps can be achieved only by computer analyses with including variable scales. In paper presentations, we need maps with at least with one meter diameter.

6. The present precision should be extended

In the application of ANOVA statistics often long distance areas of the brain are analyzed together. This type of analyses should be applied with precaution because in the same frequency band, oscillatory behavior between different recordings can be divergent. For example in frontal areas, the gamma response to visual stimulation is low, whereas gamma response in occipital areas is high. The ANOVA analysis results are, in such cases, non-significant. The same situation is also measured in alpha responses; the frontal alpha responses to sensory stimulation is very low whereas occipital alpha responses is very high. Therefore, for the fundamental construction of such maps we suggest the application of narrow regions of interests. For example, the use of 5 electrodes as arrays in occipital right areas. One must also apply a similar array for the left occipital side, since there are often also important functional asymmetries in different locations. We also suggest to build a map with sufficient information for the entire cortex shown in (Figure 5).

7. What can be the next steps to develop the CLAIR modules?

In the examples in (Figure 4a and 4b) we have described only three areas. O_2, P_4 and F_4 for imaging of all brain functions, or integrative brain functions. More detailed and distributed maps including at least 10 to 20 brain areas are needed. But this is a difficult task that requires the accumulation of more information regarding different oscillatory responses, connectivity and also variable time scale. Such presentations cannot be achieved by using classical printed illustrations. A possible method would be to use similar presentation by using geographical maps, or with variable scaling stored on a computer or internet media. The information presented in (Figure 4a and 4b) can be applied in larger structures of the cortex. Information could be retrieved by changing the scale of the large map. In this paper, (Figure 4a and 4b) includes macro presentations of such large detailed mapping.

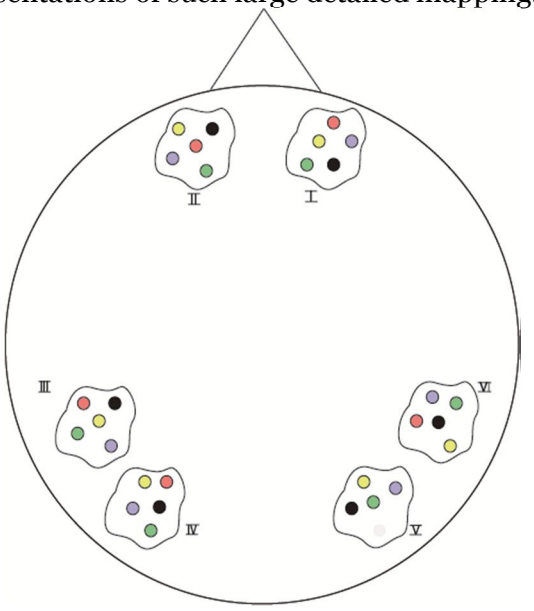

Figure 5. As it is described in the text, it is often not possible to compare left or link positions or long distance electrode positions. Amplitude of oscillatory responses are often quite different. This differentiation significantly alters the statistics. Therefore, we propose to choose an electrode constellation with 4-5 electrodes in order to obtain more precise results.

8. Conclusion

The Brodmann areas were determined firstly by anatomical presentation of functions of the brain. Why is it relevant to extend the concept of Brodman Areas?

1. In Brodmann Areas of the connections between different areas of the brain are missing. The processes of vision cannot be explained only with preliminary and secondary visual areas.

2. Not only the existence of increased electrical responses but also oscillatory components of these responses are selectively distributed throughout the whole cortex. The intensity of oscillations varies depending on the modality of stimulations. Superposition of the oscillations are also selectively distributed in different areas.

3. The most important features of CLAIR is varied connectivity. The analyses of the coherences demonstrated that upon the addition of a cognitive task is processed by a large group of brain areas and responses are usually prolonged. In simple words, the number of neural populations are increased during the performance of a task or by perception of more complex stimulation patterns.

4. Superposition of oscillations, changes in coherence, and also the degree of delayed responsiveness enables research scientists to be more exact by analyzing the functions (for example, the delay of delta in P300). Selective distribution of function related centers also shows a dynamic nature and it is not possible to find exact localization, but merely dynamic changes upon presentation of the stimulation (Luria).

5. Brodmann areas are very useful functional maps of the brain by orienting research scientists to globally learn or identify functional areas of the brain. In the study of brain oscillations, these maps are also extremely useful to choose adequate analyzing areas.

6. Brodmann areas provides a continuation of Cajal's neuron doctrine. Accordingly, the underlined principle is the existence of independent neurons, or neuron populations as functional clusters. According to Cajal, the brain is not a syncytium and functions are not a consequence of the whole brain. Barlow (1972) has even suggested that 2 or 3 cardinal neurons in the visual cortex are able to accomplish complicated functions. Başar (2011) has accumulated and explained experimental data against these assumptions. Few neurons or small populations of neurons cluster in a single area cannot be considered for the performance of a given brain function. Firstly, these facts were outlined as the functions in the whole brain. Finally, Başar (2013) has already used the expression dynamic syncytium or partial syncytium.

Three decades ago, Roy John suggested the existence of large neural populations for executive functions and named this "hyperneuron." Furthermore, (Fuster, 2013) introduced the cognits for presenting functional units, functional modules for presentation of cognitive functions.

7. The expression "CLAIR areas" is a consequence of these earlier judgments, or theories. But relieves extended measured neurophysiological parameters as superposition of brain oscillations, topological differentiations and degree of connectivity (coherences) between different brain structures. Additionally, in the future, degrees of phase-locking and timescale must be added to these maps.

8. There are huge differences in frequency composition of different parts of the cortex upon application of sensory or event related stimulations. These findings add highly to the significance of CLAIR maps.

9. CLAIR differentiations by means of partial CLAIR maps is also indicated in case of diseases such as Alzheimer and Bipolar Disorder. It can be anticipated that such maps can be also useful for physician to differentiate diseases.

10. The preliminary CLAIR maps and their current rough structure are based on present experimental data; therefore, we need analyses with exact numerical data and also, by considering measurements under all concepts and measurements after following the application of drugs in patients.

11. The present paper is not a final study and needs several new steps and addition of more experimental data, as it was the case in the development of the concept of Brodmann areas. We propose in future the expression "modules with different size and extensions."

12. In the present report, the most important step towards brain oscillations and functionality in the brain consists in building maps by combining oscillatory responses and connectivity in the whole cortex. The inclusion of the functional activity of the cerebellum could not yet be achieved in CLAIR maps.

13. Furthermore, we did not take care of the exact time localization of the oscillatory responses. This can be done only after analyses of phase spectra. This can be performed by changing the locations of oscillatory response bars in the alpha, beta, delta, theta frequency windows.

14. Additionally, important additive information is intertrial coherence analyses. The addition of ITC could be achieved possibly with three dimensional maps.

15. In the present paper, the proposal the develop CLAIR maps are based on neurophysiological empirical findings including several EEG oscillations, and connectivity. It is assumed that in this way a relevant progress for functional brain maps will be achieved. However, we do not assume that the anatomical importance of Brodmann areas and also findings of Penfield should be discarded.

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