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Review

The alpha-theta-gamma (ATG) switch: Toward unified principles of cortical processing

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ABSTRACT

Neural oscillations and their synchronization among brain areas are associated with numerous sensory and perceptual processes, but new theories to integrate the many empirical findings are still needed. Based on a comprehensive review of animal and human literature, we probe and introduce a neurophysiological framework to explain how coordinated cross-frequency and inter-regional oscillatory cortical dynamics underlie typical and atypical brain activation, and the formation of distributed functional ensembles supporting cortical networks underpinning sensation and perception. We propose that local regional activation by an external stimulus via a sensory pathway entails (i) attenuated alpha (8-14 Hz) and increased theta (4-8 Hz) and gamma (30-50 Hz) oscillatory activity, and (ii) increased interactions among theta and gamma rhythms. These local dynamics also mediate the integration of activated neural populations into large-scale functional assemblies through neuronal synchronization. We also discuss evidence that alpha-theta-gamma dynamics emerging from thalamo-cortical and cortico-cortical interactions may be implicated in cognition across diverse contexts, and that the disruption of such processes is implicated in numerous neurological and neuropsychiatric conditions.

KEYWORDS: alpha, theta, gamma, neural oscillation, neural synchrony, local dynamics, large-scale assemblies, perception, cognition, neurological conditions

ABBREVIATIONS

ATG	:	Alpha-theta-gamma
BOLD	:	Blood-oxygen-level-dependent
CC	:	Cortico-cortical
CT	:	Cortico-thalamic
EEG	:	Electroencephalography
GABA	:	Gamma-aminobutyric acid
Hz	:	Hertz
iEEG	:	Intracranial electroencephalography
MEG	:	Magnetoencephalography
MRI	:	Magnetic resonance imaging
TC	:	Thalamo-cortical
TCD	:	Thalamo-cortical dysrhythmia
TT	:	Thalamo-thalamic

1. Introduction

Sensory, perceptual, motor and cognitive acts are associated with oscillatory changes within task-relevant cortical brain regions, as well as alterations in functional and effective connectivity between those regions associated with neuronal

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synchronization [1-4]. It is increasingly appreciated that the selective activation of a specific constellation of distributed neural populations, and their transient integration, are closely associated with action, perception, and thought [2, 5, 6]. Recording methodologies with sufficient temporal resolution to measure fast (>1 Hz) neural oscillations, such as electroencephalography (EEG), intracranial electroencephalography (iEEG) and magnetoencephalography (MEG), have shown that brain dynamics within and between regions often differ markedly across frequencies, and that brain rhythms often interact across widely separated frequency ranges [7-15]. It has further been reported that cross-frequency interactions may play an important role in local processing within the thalamus and neocortex, as well as information transfer between them [16]. Strong commonalities in rhythmic network properties have been observed across recording techniques and task demands, but strong neuroscientific theories to situate such observations within a unified framework that has direct relevance to the explanation of neuropathologies remain scarce.

2. Inter-regional oscillatory and coordinated cross-frequency dynamics: the emergence of the ATG switch

Based on the current literature, we propose that a unified set of oscillatory mechanisms underpins the activation of cortical regions and their integration into distributed functional ensembles. Specifically, we postulate that when a functionally distinct brain region is recruited during sensory/perceptual processing, and possibly also during motor or cognitive processing, local rhythms in that brain area transition from a predominantly resting/inhibited alpha-band (8-14 Hz) oscillatory state toward increasing theta-band (4-8 Hz) and low gamma-band (30-50 Hz) activity, accompanied by enhanced cross-frequency coupling between theta and gamma oscillations. These local oscillatory dynamics are enmeshed with mechanisms mediating their integration into functional networks via enhanced synchronization among task-activated regions. Such mediation depends on interactions between lower- and higher-frequency cortical rhythms [17], in which theta-gamma mechanisms play a role in sculpting communication (information and control) among distributed, coactive constellations of neurons forming transiently-organized, functional brain networks [6, 10]. We refer to this transition of functional network properties as the 'alpha-theta-gamma switch', or ATG switch. We contend that this brief dynamic switch, spanning a time period of a few hundred milliseconds and observable in the animal/human literature, represents a fundamental mechanism for active cortical processing and further can explain some aspects of alterations in brain activity as a result of neuropathology.

2.1. Local alpha oscillations and inhibition

Local alpha oscillations are classically thought to reflect cortical inhibition [18] and/or idling [19], as local alpha power reductions have been observed following stimulus presentation in various sensory modalities [18]. Such reductions have also been observed in intermodal attention [20], visuospatial attention [21], and attention to 'color' vs. 'motion' [22]. Local desynchronization of alpha rhythms over primary cortex is also associated with active motor control [23] and perceptual processing [24]. Importantly, modulations of alpha power within sensorimotor cortex predict performance, spike timing, and firing rate [25]. Further, induced hypersynchronous ongoing frontal activity in the alpha range during sedation is closely associated with, or even responsible for the loss of conscious perception [26].

It has also been reported however, that increases in synchronization of alpha oscillations between distant cortical regions may be related to the establishment of long-range networks further relating to working memory retention [13, 27] and maintenance of attention at a spatial location [11]. Since resting alpha rhythms are well known to arise mainly from occipital areas, such synchronization may reflect an expansion of alpha oscillations into cognitive areas with subsequent distributed local desynchronization relating to local cortical cognitive activations [28]. Such results and others indicate that alpha oscillations primarily reflect fundamental mechanisms of cortical idling and inhibition that function to direct information flow within brain networks across diverse contexts [28, 29].

2.2. Local gamma and theta oscillations and cortical activation

Local increases in gamma-band activity have been linked to active processing within cortex across

numerous contexts, consistent with the view that they play a critical role in attention and memory [30], as well as a more general role in all cortical sensory and cognitive processing [5, 31]. Sensory stimulation produces gamma activation [32, 33], as does perception [34], object recognition and representation [35], and short-term memory retention [36]. Processes that have been reported to reduce local alpha activity are also associated with increased local gamma activation [37, 38]. Local increases in gamma power likely arise through synchronization of local field potentials across proximal cortical columns [39] integrated into a task- and/or percept-dependent functional ensemble [6, 40]. As alpha-desynchronization occurs across large areas of cortex relative to the more spatially complex coincident increases in gamma power [41], transitions of local population dynamics from alpha toward a gamma oscillatory state may mediate segregation of neural populations into functional assemblies into which elements relevant for required cortical computations are selectively integrated.

Local theta rhythms have been related to task-dependent processing in both hippocampus and neocortex [42]. The relationship between cortical theta oscillations and active processing is perhaps best documented in working memory paradigms [43]. Local theta activity has also been implicated in other cognitive processes including selective attention [44], navigation [45], and long-term memory processes [46]. Given that alpha oscillations are locally suppressed in many of these same contexts, it is likely that task-dependent activation within a cortical region involves a shift in the dominant frequency of rhythmicity from the alpha band to the theta band.

2.3. The ATG switch: A mechanism of cortical activation

If the cortex is a finely-tuned dynamic network in which interactions among oscillatory rhythms sculpt the flow of information and control, then the above literature (and others not cited here) is consistent with a general framework supporting information processing in the brain: activation of a local neural population involves a shift away from the dominant alpha rhythm toward both lower frequency (theta) and higher frequency (gamma) oscillations (Figures 1A, 1B, 1C) [47-49]. Whereas alpha band idling can be associated with a noncoding global attractor [50]; converging evidence indicates that theta and gamma oscillations participate in a unified local dynamic supporting cortical information processing. Human iEEG reveals that the amplitude of some cortical gamma rhythms is locked to the phase of theta oscillations, and that this coupling is reinforced in task-relevant brain areas during cognitive and perceptual processing [51]. Theta-gamma coupling has also been reported in a variety of perceptual and cognitive processes based on noninvasive recordings [9, 10, 14, 52] (Figure 1E). This theta-gamma relationship is not unique to cortex, but also plays a vital role in hippocampal function [53]. It may be the basis for a 'neural code' by which the brain represents ordered sequences of items in memory [54]. Such findings have led to the hypothesis that cross-frequency coupling plays a critical role in cortical processing in health and disease [7, 55, 56, 57]. These findings, together with evidence presented earlier, indicate that activation of a cortical region involves (i) partial slowing from alpha to theta, (ii) enhanced area-specific theta- and gamma-band oscillatory activity, (iii) coupling between theta and gamma oscillations, which mediates task-dependent processing, and (iv) resulting partial global desynchronization of alpha rhythms. This can be described as a switch from a local resting/idling alpha oscillatory state to a task-specific active mode dominated by interacting theta and gamma rhythms, within a stimulus- and task-relevant set of distinct local neural ensembles, spanning a few hundred milliseconds: the ATG switch.

2.4. The ATG switch and cortical network dynamics

Interactions between low- and high-frequency oscillations have been proposed to mediate the integration of local neural activity into large-scale networks [17]. This view is supported by findings that long-range gamma connectivity is modulated by theta rhythms during conscious recollection [58], and theta phase modulates inter-regional gamma synchronization across diverse contexts including visual perception [10] and auditory attention control [14] (Figure 1E). Long-range synchronization of gamma oscillations has been implicated in functional network integration supporting selective attention [14, 38], working memory [59] and perception [10, 60] (Figure 1D). Mediation of gamma oscillatory neuronal assemblies by theta

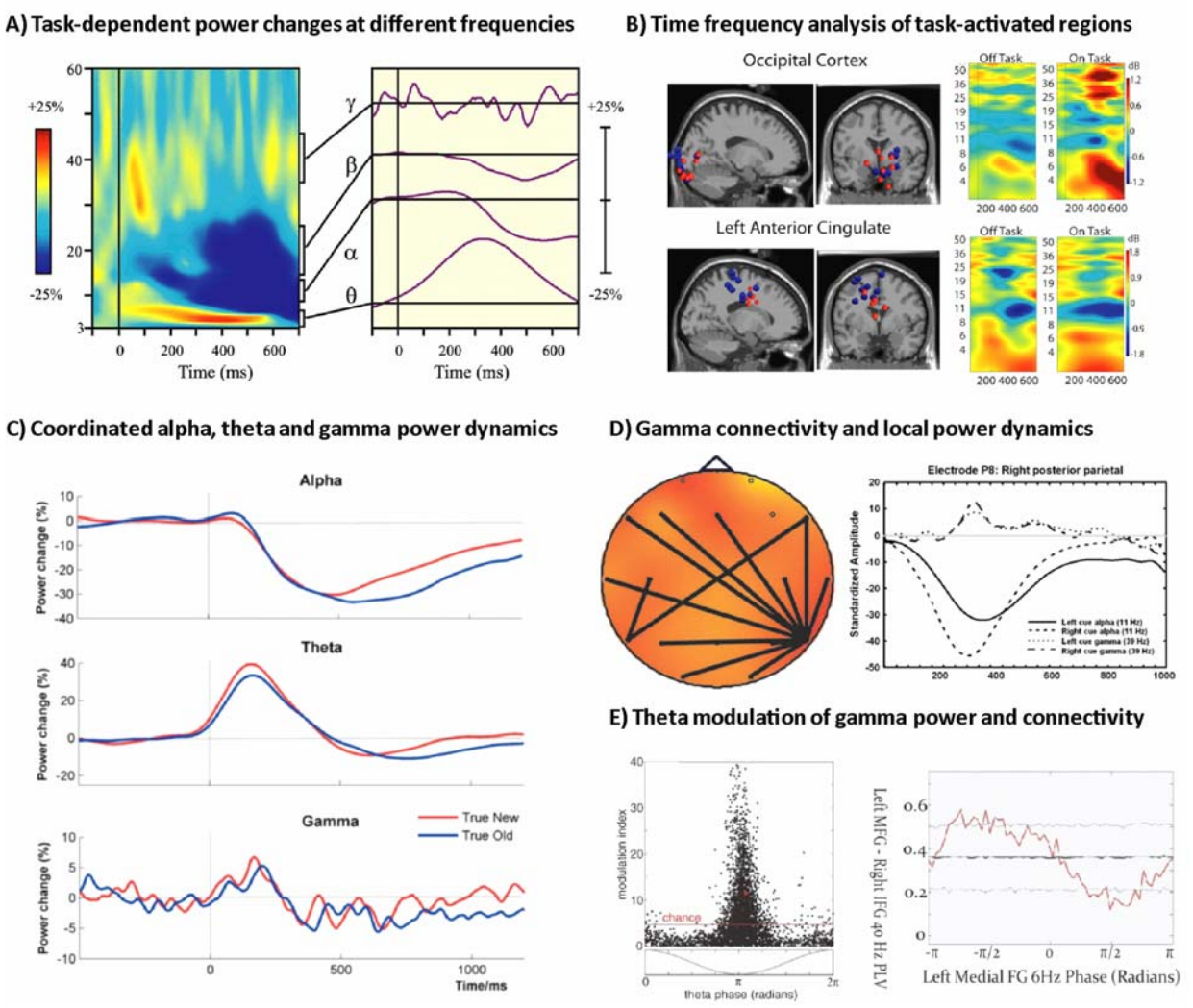

Figure 1. Neurophysiological examples of the ATG switch: **A)** Prolonged alpha desynchronization in parallel with theta synchronization and periodic, recurrent gamma activation during auditory/visual discrimination processing using EEG recordings. Left: Time-frequency spectrogram visualizing changes in power at different frequencies (Hz) over time; Right: Event-related spectral changes within frequency bands over time (modified with permission from [47]). **B)** Sustained alpha desynchronization in parallel with a prolonged theta-gamma activation/synchronization is prominent in specific sensory (occipital cortex) and non-specific or non-sensory (left anterior cingulate) cortical areas during a sustained attention to response task using EEG recordings. Red and blue dots in leftmost column represent individual subjects' dipole locations of independent components from two separate experiments (modified from [48]). **C)** Event-related power changes (averaged across Fz, Cz, Pz, and Oz EEG channels) in various frequency bands after the onset of a stimulus in a face recognition memory task. Sharp increases in theta and gamma bands are followed by a more sustained decrease in alpha band (modified with permission from [49]). **D)** Significant lateralized gamma-band connectivity between occipital cortex and other distant brain areas (black lines in left panel) is greatest when alpha power is decreased and gamma power is increased in occipital cortex (right panel; modified from [38]). **E)** Gamma power (left panel) and gamma connectivity (right panel) are modulated by theta phase (modified with permission from [6, 10]).

rhythms may integrate network dynamics across longer distances, as the longer period of the theta rhythms makes its synchronization resilient against time delays.

Selective attention represents an area of research for which all elements of the ATG switch have been well established. During covert attention orienting, alpha oscillations are desynchronized, indexed

by reduced power, in cortical regions relevant to processing stimuli at the attended location [21], and this has been related to enhanced performance [61]. Increased theta activity is also evident in these regions [44]. Selective attention has also been shown to increase local gamma activation using both invasive [37] and noninvasive [62] measures, and these increases in gamma power are coincident with task-dependent alpha desynchronization [38] (Figure 1). Attention control has also been shown to enhance gamma-band synchronization between cortical regions [38, 63, 64]. Recently, we demonstrated increased local gamma amplitude and increased inter-regional phase locking in the gamma band in a network of theta-activated brain regions during attention control [14]. Moreover, gamma-band synchrony among theta-activated regions was found to be modulated by the phase of cortical theta oscillations. We propose that attention orienting constitutes an instance of the ATG switch, wherein subsets of task-related brain areas shift the frequency of their dominant rhythm from the alpha to the theta band, and through theta/gamma interactions, these regions increase local gamma power and enhance inter-regional gamma-band phase coupling. Thus, the ATG switch may be a manifestation of a mechanism of cortical rhythmicity underlying the dynamic selection and integration of distributed neural populations into functional Hebbian cell assemblies underlying attention control, mediated by co-activation and gamma frequency phase synchronization [6].

Task-dependant inter-regional synchronization has also been observed at other frequencies including alpha [13], and cross-frequency interactions of oscillatory connectivity have been observed [8], suggesting that hierarchically nested network oscillations encapsulated in the harmonics of n:m phase locking of theta and gamma rhythms may serve to organize cortical information flow [65].

2.5. Neurophysiological foundation of the ATG switch

Thalamo-cortical interactions are important and involved in the generation of alpha-, theta- and gamma-band oscillations. Mathematical modeling of the thalamo-cortical system showed that the dynamics of the cortical networks were turbulent and desynchronized when intrinsic thalamic activity was excluded from the model [66, see also 67]. The onset of a thalamic pacemaker input organized the system into a more coherent spatio-temporal behavior and further provided evidence for the significance of coupling and connectivity of oscillatory activity within thalamo-cortical systems.

Further, disruption of thalamo-cortical connectivity can induce deceleration of cortical alpha oscillations toward the theta frequency range [68]. Either excess inhibition or dysfacilitation in thalamus causes the generation of low-threshold calcium spike bursts by thalamic neurons, in both non-human animals [69] and humans [70]. Thalamic cell hyperpolarization and generation of low-frequency thalamic oscillations occur in the presence of these bursts [71]. This produces a shift of oscillatory frequency from alpha to theta (similar to what is observed during sleep), the result of a resonant interaction between thalamus and cortex [72, 73]. It is important to note that slowing of oscillations within thalamus is mostly observed in the delta (1-4 Hz) range in invasive animal studies [71], and can be observed during thalamic recordings from neurosurgical patients [70], while a “broader” slowing in the delta/theta range, and most dominantly in the theta range (4-8 Hz) can be observed from cortical MEG/EEG recordings in humans, due to thalamo-cortical network interactions [7]. The shift from alpha to theta band range is generally reported as a persistent cortical slowing, observed predominantly in the theta frequency band, measured using MEG or EEG in neurological as well as psychiatric pathologies, due to either excess inhibition (i.e. Parkinson’s disease) or dysfacilitation (i.e. chronic pain) on the thalamo-cortical system [7, 67, 74], or as a slight slowing in mild traumatic brain injury [75]. Such slowing across thalamo-cortical networks also induces cross-frequency interactions relating to an enhancement and coupling of cortical theta/gamma rhythmicity, probably via slowing-induced cortical dysinhibition [5]. Animal studies have also confirmed that injection of slow wave activity into thalamus induces activation of locally segregated cortical gamma-band oscillations [76].

Such neurophysiological mechanisms linking oscillatory slowing and cross-frequency interactions may further provide an explanation for the time course of such coordinated changes in oscillatory power in the healthy brain. Careful inspection often reveals that theta-gamma changes appear to precede alpha desynchronization (Figure 1C). Since gamma-

oscillatory ensembles typically incorporate fewer neurons than do alpha oscillations [41], it is likely that task-processing integrates a particular subset of task-relevant neurons at gamma and theta rates, subsequently causing partial desynchronization of alpha oscillations across the activated region. This may be further explained in detail by the thalamo-cortical network model [40, 67, 77], in which an iteration of task-related partial slowing into the specific thalamo-cortical system via cortical layer IV activates local task-relevant neurons at gamma and theta rates with a slightly delayed alpha desynchronization. This is followed by further slowing into task-related non-specific thalamo-cortical networks via layer I combined with further ongoing alpha desynchronization. Activation of task-related cortical network dynamics, via layer I throughout cortex, at gamma and theta rates in a timely manner [67], then integrates 'sensory' content into global 'cognitive' context [40] or 'core' into 'matrix' [77].

2.6. Pathological instantiation: a permanently altered ATG switch

Typically, the ATG switch operates only transiently for a few hundred milliseconds depending on the required information processing in a specific context. There is reason to believe, however, that under some (pathological) circumstances it can become abnormally "stuck in the on position", resulting in persistently altered oscillatory dynamics within thalamo-cortical networks, regardless of processing needs. Thus, persistent slowing to theta frequency, coincident with enhancement of local theta- and gamma-band rhythmicity, coupling between gamma and theta oscillations, and global alpha desynchronization, may represent a permanently altered ATG switch, and permanently altered connectivity dynamics across a patient's symptom-specific distributed networks. Such a pathological instantiation of the ATG switch may further provide a more detailed understanding for the earlier described thalamo-cortical dysrhythmia [7].

Evidence relating oscillatory aberrations to positive symptoms in several neurological and psychiatric populations supports the notion that the abnormal brain activity involves a transition from an alpha oscillatory state to an activated theta/gamma mode. This phenomenon is known as 'thalamo-cortical dysrhythmia' (TCD) [7], and may reflect a pathological instantiation of the ATG switch. Thalamo-cortical dysrhythmia was discovered when MEG was employed to investigate spontaneous (resting) cortical oscillations in neurological and neuropsychiatric populations. This research demonstrated that in several pathological conditions, including neurogenic pain, Parkinson's disease, and others, resting-state peak-power oscillatory frequency was slowed from an alpha to a theta rate, gamma power was increased, and cross-frequency coupling was observed among theta and gamma rhythms [7]. This is understood to result from either a deafferentation of thalamus (i.e. chronic pain) or an excess of inhibition of thalamic activity (i.e. Parkinson's disease) [7, 78]. The debilitating nature of many of these conditions is not surprising in this light, given how profoundly enmeshed thalamic and thalamo-cortical circuits are in the generation of cognition, perception and consciousness [5, 32, 67, 79, 80].

Recent imaging evidence indicates that the specific nature of positive symptoms varies across conditions according to the cortical regions affected [74]. Rather than functioning in a "normal" transient and task-dependent fashion, the ATG switch in such patients may be permanently, and inappropriately, activated within these pathology-related networks because of persistent inhibition or dysfacilitation of symptom-specific thalamic areas [70]. Since the initial research, other studies have confirmed several aspects of reported oscillatory abnormalities in various conditions. Enhanced theta and gamma power have been described in patients suffering from neurogenic pain [73, 81] and Parkinson's disease [72]. Moreover, the implication of dysrhythmic thalamo-cortical interactions and coherence between thalamic and cortical areas is supported by observations made using surface electrodes and surgically implanted electrodes in patients with Parkinson's disease [72] and neurogenic pain [73]. In this view, focal increases in gamma, which are implicated in perception and cortical activation, induce the (illusory) experience of positive symptoms such as pain [81], or the perception of a sound (tinnitus) [82, 83], depending on the anatomical location of the excessive gamma oscillations [67].

2.7. The ATG switch as a fundamental mechanism

Based on the current literature presented, we have reasons to believe that in normal brain function

the ATG switch represents a fundamental mechanism mediating network activation and integration, underlying the transition of local oscillatory activity from an idling or inhibited state to one promoting selective information processing (Figure 2). This allows the task-dependent integration of well-trained specific local circuits into long-range connectivity across the entire brain, by integrating "content into context" or "core into matrix" [67]. Both specific and non-specific thalamo-cortical conjunctions have been confirmed by direct recordings from animals [84]. Moreover, the interaction between the specific and non-specific thalamic loops supports the idea that, rather than simply being a relay station, the thalamus represents a hub from which any site in the cortex can communicate with any other site(s) [79, 80, 85]. MEG has also provided further evidence for bi-directional causality within the thalamo-cortical paralimbic network related to autobiographic memory retrieval and self-awareness [86], indicating the involvement of such dynamics among cortico-thalamo-cortical networks. The ATG switch, then, may represent a fundamental mechanism within thalamo-cortical networks underlying sensory, perceptual, and cognitive processing. These dynamics may further emerge from cortico-thalamic feedback inhibition and subsequent cortical GABA-ergic disinhibition relevant for gamma

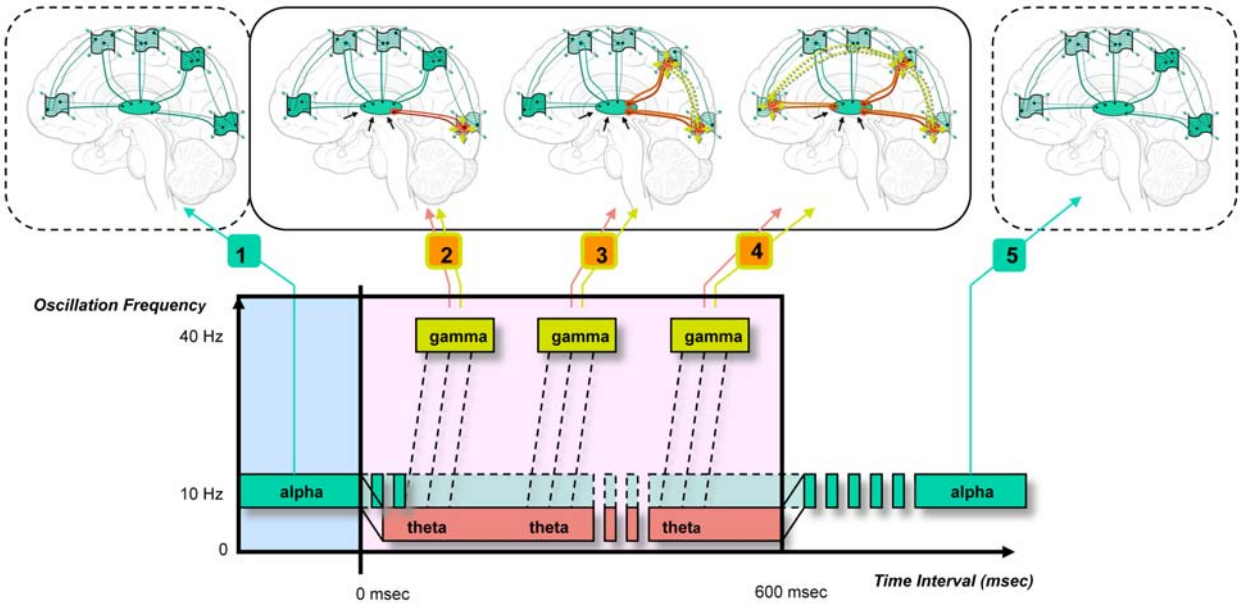

Figure 2. The conceptual model for the ATG switch: Proposed neural mechanisms to functionally activate a local network and mediate the assignment of transient functional connectivity within distributed networks in a task-specific selective way. (1) The classical resting state (alpha; shown in green) spanning a large brain space and concentrated over occipital areas (darker green); (2) following stimulus, or internal/intrinsic input from CT feedback (during an activated task-mode or during 'an internally activated' spontaneous or default-network mode) there is a brief inhibition on task-specific part of thalamus, resulting in a brief slowing of that part of thalamus and the related task-specific TC network to the theta band frequency (shown in red). This will, via cortical layer IV, further induce a dysinhibition and increased local theta-driven cortical gamma-band synchronization (shown in yellow) and coupling (correlated theta/gamma band activity). In parallel, this induces a slightly-delayed and related partial background alpha desynchronization (shown in light green) due to slowing (shift from partial alpha to theta); (3 and 4) further sequential task-specific intrinsic partial inhibition (probably through CT or TT networks) and induced slowing to theta band in task-related non-specific TC networks via layer I, inducing additional or different spatially segregated local theta-driven gamma-band synchronization and coupling, further mediating functional long-range cortical network interactions and connectivity by theta-gamma synchronization, probably involving related CC/CT/TC loops; (5) after termination of those brief spatio-temporal segregated inputs/inhibition on the TC network, theta frequencies restore back to alpha frequency band and baseline-mode (resting state or non-activated mode). In neuropathological conditions, this ATG switch will be symptom-specifically and permanently activated, resulting in permanent theta/gamma band correlation (in any combination of scenarios 2, 3, or 4) [see 7, 67].

oscillations mediating information processing and network integration.

2.8. GABA-ergic modulation, brain network organization and the ATG switch

The conceptual model of the ATG switch, Figure 2, with proposed brief and selective inhibition to alter functional states of networks relating to perception and cognition, adds to our understanding of selective network area activation through inhibition. This role for neuronal inhibition was earlier suggested by Buzsáki and colleagues, who postulated that long-range-projecting inhibitory GABA-ergic neurons might be an ideal substrate to precisely coordinate brain activity between distant cortical brain regions [87]. Recent findings in animals have indeed identified and characterized long-range GABA-ergic neurons that provide bi-directional hippocampal-entorhinal inhibitory connectivity and preferentially target GABA-ergic interneurons [88], to modulate neural activity through disinhibition (inhibitory inhibition). In parallel, a series of studies of human brain structure reports on the segregation (elaboration and assembly) of semi-autonomous building blocks, defined by genetics [89]. This incredible structural complexity underlies functional segregation in the cerebral cortex, a mosaic of hundreds of interconnected and microscopically identifiable areas that controls perception, cognition and behavior. Various studies find unifying hierarchical and geometric rules behind the organizational details, such as the geometric structure of the brain fiber pathways [90], or the hierarchical genetic organization of human cortical surface area [91]. Such studies may further relate to and shed light on the detailed organization and significance of neural hubs [92]. Taken together such evidence indicates that a mechanism of neural inhibition that promotes consequent selective coordination of various task-specific brain areas is quite plausible, and we propose that the ATG switch may play a major role in such selective activation dynamics. Indeed, gamma oscillations and their synchronization may be further related to interactions of cortical pyramidal neurons and interneurons [93, 94].

2.9. Conceptual model of the ATG switch

The conceptual model of the ATG switch (Figure 2), and all the related literature that supports it, may challenge the dominant view in neuroscience regarding sensory stimulation and cortical activation. The ATG switch may rather suggest that sensory stimulation or cognitive processing results in "brief inhibition" in the thalamo-cortical network, causing brief slowing and resulting in local synchronization in the theta- and gamma-bands and coupling of theta/gamma oscillations integrating local and distributed networks. This is consistent with the view that upon stimulation the brain may not undergo an activation *per se*, but rather a local inhibition and related cortical disinhibition and synchronization/ integration of existing ongoing intrinsic activity. This idea represents a more specific form of the proposal by Lashley [95] and later by others [40, 96] that new stimuli interact with ongoing brain activity to integrate external information and generate new activity patterns rather than simply stimulating new activity in a quiescent brain.

2.10. Thinking beyond synchrony

We propose that the ATG switch reflects a basic biological mechanism that generally implicates a switch from "resting state or stand-by mode" to the activation of local and task-related distributed functional networks relating to sensory perception and cognition, and thus represents a fundamental attribute of oscillatory dynamics that arises from network properties in thalamo-cortical and cortico-cortical circuits. Further, its malfunction is proposed to be responsible for a range of neurological pathologies. This framework opens new possibilities for challenging strategies of signal processing analysis in dynamic imaging modalities (>1 Hz) beyond brain network connectivity and causality, focusing on activation and inter-regional coordination patterns across 5 dimensions, within 3-dimensional space and across frequency and time. Finally, it further suggests targets for better diagnostic biomarkers and new treatments of neurological disorders.

3. Outstanding questions

Based on the literature presented here (and other not cited), we propose the ATG switch as an initial step towards a basic biological mechanism that has to be further explored and expanded in detail. There are some outstanding questions yet to be resolved by future research, including multimodal structural and functional brain imaging and clinical assessments. Such questions include:

- Does the ATG switch apply to neural activation in all brain systems and all tasks? What is special or different about activity that does not conform with the ATG switch?
- How does the beta rhythm relate to the ATG switch, as beta oscillations are frequently reported to be desynchronized as well as alpha oscillations? How do higher frequency oscillations, such as ripples, and lower frequency traveling or standing waves in the brain, relate to the refinement of the ATG switch?
- How does the ATG switch exactly relate to the BOLD signal measured by functional MRI, or to the evoked responses measured by EEG and MEG?
- What is the relation between parameters of the ATG switch and individual differences in sensory, perceptual and cognitive ability? How can the ATG switch be reliably quantified?
- How does the ATG switch develop throughout infancy and childhood? How are these changes related to sensory, perceptual and cognitive development?
- How does the ATG switch relate to the predisposition of certain brain systems to oscillate at particular frequencies, such as the prevalence of alpha rhythms in occipital and Rolandic cortex, or the prevalence of hippocampal theta?
- How does the ATG switch relate to the specificity of the various positive symptoms observed in neurology? Do some neurological symptoms not relate to the ATG switch?
- Does the development of the ATG switch relate to the critical stages of child development and the early occurrence of neurological symptoms throughout child infancy and childhood?

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CONFLICT OF INTEREST STATEMENT

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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