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The Intrinsic Network Dynamics Related to Abnormal Delta Rhythm in Consciousness Disorders (Short Review)

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Summary

Aim: to explore the pathophysiological mechanisms and clinical significance of delta rhythms (⩽4 Hz) in disorders of consciousness (DOC), including coma, unresponsive wakefulness syndrome (UWS), and minimally conscious state (MCS), as biomarkers for diagnosis, prognosis, and therapeutic targeting.

Materials and Methods. A narrative review was conducted, focusing on experimental and clinical findings related to delta rhythm generation and modulation in the disorder of consciousness (DOC). Emphasis was placed on thalamo-cortical interactions, cortical inhibition, neuromodulatory deficits, and the role of glial cells, neuroinflammation, and metabolic disruptions. Quantitative EEG analysis and advanced neuroimaging were highlighted as key tools for assessing delta activity.

Results. Delta rhythms were found to dominate EEGs across DOC states, with high-amplitude global activity in coma and low-amplitude activity in UWS, indicating cortical suppression and thalamocortical disconnection, respectively. In MCS, reduced delta power and improved connectivity correlated with intermittent purposeful behavior. Therapeutic interventions, including TMS, tACS, and pharmacological agents, showed potential for modulating delta rhythms. Additionally, stochastic resonance emerged as a novel mechanism to stabilize neural networks through noise.

Conclusion. Delta rhythms serve as crucial biomarkers in DOC, offering diagnostic, prognostic, and therapeutic value. Multimodal approaches that integrate EEG, neuroimaging, and mechanistic studies are essential for deepening understanding and improving clinical outcomes in DOC management.

Keywords: Delta rhythm; EEG; disorders of consciousness; neural networks; delta-alpha rhythms; neuroimaging

Conflict of interest. The authors declare no conflict of interest.

Внутренняя динамика сети, связанная с аномальным дельта-ритмом при нарушениях сознания (краткий обзор)

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Резюме

Цель: изучить патофизиологические механизмы и клиническую значимость дельта-ритмов (⩽4 Гц) при нарушениях сознания, включая кому, синдром безответного бодрствования (вегетативное состояние) и состояние минимального сознания (СМС), в качестве биомаркеров для диагностики, прогноза и целенаправленной терапии.

Материалы и методы. Провели краткий обзор результатов экспериментальных и клинических исследований по изучению генерации и модуляции дельта-ритма при нарушениях сознания. Особое внимание уделили таламо-кортикальным взаимодействиям, кортикальному торможению, нарушениям нейромодуляции, а также роли глиальных клеток, нейровоспалению и метаболическим нарушениям. Количественный анализ ЭЭГ и усовершенствованную нейровизуализацию выделили в качестве ключевых инструментов для оценки дельта-активности.

Результаты. Установили, что дельта-ритмы доминируют на ЭЭГ при всех состояниях нарушенного сознания, при этом глобальная активность с высокой амплитудой наблюдается при коме, а активность с низкой амплитудой — при вегетативных состояниях, что, соответственно, указывает на подавление активности коры головного мозга и таламокортикальное отключение. При СМС снижение амплитуды волн дельта-ритма и улучшение связи коррелировали с периодическим целенаправленным поведением. Терапевтические вмешательства, включая транскраниальную магнитную стимуляцию, транскраниальную стимуляцию переменным током и фармакологические препараты, демонстрировали потенциал для модуляции дельта-ритмов. Кроме того, стохастический резонанс стал новым механизмом стабилизации нейронных сетей, проходящим сквозь помехи.

Заключение. Дельта-ритмы служат важнейшими биомаркерами состояний нарушенного сознания и представляют диагностическую, прогностическую и терапевтическую ценность. Мультимодальные подходы, объединяющие ЭЭГ, нейровизуализацию и механистические исследования, необходимы для углубления понимания и улучшения клинических результатов при лечении пациентов в состоянии нарушенного сознания.

Ключевые слова: дельта-ритм; ЭЭГ; нарушения сознания; нейронные сети; дельта-альфа-ритмы; нейровизуализация

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Introduction

Disorders of consciousness (DOC), including coma, unresponsive wakefulness syndrome (UWS), and minimally conscious state (MCS), represent complex conditions involving disruptions in neural networks. Delta rhythms are prominent in DOC and indicate underlying pathological states. Understanding the mechanisms and implications of delta activity is essential for improving diagnostics, prognostics, and therapeutic approaches. This review synthesizes recent advances in delta rhythm research, emphasizing their mechanistic underpinnings and clinical relevance [1–4].

Mechanisms of Delta Rhythm Generation

Delta rhythms originate from dynamic interactions within the thalamo-cortical circuitry, influenced by [1, 5–8]:

- Thalamic contributions: шntrinsic oscillatory properties of thalamocortical neurons, mediated by T-type calcium channel dynamics, play a pivotal role in delta generation. Aberrant oscillations within thalamic relay neurons have been linked to hyperpolarized membrane states, resulting in the pathological emergence of delta rhythms.
- Cortical dynamics: cortical neurons contribute to delta activity through synchronized hyperpolarization states, facilitated by GABAergic inhibition. Recent studies have shown that disruptions in interneuron networks can exacerbate the desynchronization seen in DOC.
- Neuromodulatory inputs: cholinergic and dopaminergic systems modulate delta rhythms, with deficits in these pathways observed in DOC patients. Furthermore, noradrenergic and serotonergic systems may indirectly influence delta activity by modulating the arousal network [9–13].
- Role of glial cells: emerging evidence suggests that astrocytes and microglia contribute to rhythm generation by modulating synaptic activity and clearing metabolic byproducts. Neuroinflammation, a common feature in DOC, may alter glial function and impact delta rhythm dynamics [14–16].

Delta Rhythms in Coma

Coma, a profound state of unresponsiveness, is often characterized by pronounced delta activity [17–20] Key features include:

- Global cortical suppression: coma patients typically exhibit high-amplitude, generalized delta rhythms on EEG, reflecting widespread cortical and subcortical dysfunction.
- Thalamic dysfunction: reduced thalamic input in coma is associated with the dominance of slow-wave activity, disrupting normal thalamo-cortical interactions.
- Prognostic insights: while persistent delta activity in coma is indicative of severe brain dysfunction, the gradual re-emergence of faster rhythms may signal recovery potential. Studies have highlighted that early shifts in EEG patterns can predict outcomes in coma patients.

Delta Rhythms in Different DOC States [1, 3, 21]

Distinct delta rhythm profiles differentiate coma, UWS, and MCS:

- *Unresponsive wakefulness syndrome (UWS):* Characterized by widespread, high-amplitude delta activity, reflecting severe cortical disconnection and reduced thalamo-cortical communication.

- *Minimally conscious state (MCS):* Lower delta power and greater functional connectivity compared to UWS, indicating partial preservation of cortical networks. This preservation is often associated with sporadic evidence of purposeful behavior.
- *Emerging patterns in recovery:* Patients transitioning from DOC states often exhibit gradual reductions in delta power, accompanied by increased alpha and beta rhythms, indicative of cortical reorganization.

Diagnostic and Prognostic Value [22–25]

Delta rhythms serve as biomarkers for:

- Diagnosis: Quantitative EEG measures, such as delta power, coherence, and cross-frequency coupling, aid in differentiating DOC states. Combining delta metrics with machine learning approaches has shown promise in improving diagnostic accuracy.
- Prognosis: Changes in delta rhythm characteristics over time correlate with recovery potential, informing clinical decision-making. For instance, a shift from global delta dominance to localized delta activity may indicate partial network restoration.

Therapeutic Implications [1, 20, 26, 27]

1. Neuromodulation: Techniques such as transcranial magnetic stimulation (TMS) and transcranial alternating current stimulation (tACS) target delta activity, showing promise in restoring cortical network function. The use of personalized stimulation protocols, based on individual EEG profiles, may enhance therapeutic outcomes.
2. Pharmacological Approaches: Agents modulating T-type calcium channels or enhancing cholinergic activity offer potential for delta rhythm normalization. Recent trials involving ampakines and GABA-A receptor modulators have demonstrated preliminary efficacy in altering delta dynamics.
3. Noise Modulation: Harnessing the paradoxical stabilizing effects of noise, such as through stochastic resonance, represents an emerging therapeutic avenue. Experimental studies suggest that introducing controlled noise can enhance signal transmission in impaired neural circuits.

Integration with Multimodal Biomarkers [28–32]

Combining delta rhythm analysis with neuroimaging modalities enhances the understanding of DOC pathophysiology. For instance:

- Functional MRI (fMRI): reveals connectivity patterns linked to delta activity, providing insights into network-level disruptions.
- Diffusion Tensor Imaging (DTI): assesses white matter integrity associated with rhythm generation. Studies have shown that reduced fractional anisotropy in thalamic and cortical regions correlates with elevated delta power.
- PET Imaging: investigates metabolic abnormalities that may underlie delta rhythm alterations, such as glucose hypometabolism in key brain regions.

Future Directions

Key areas for further exploration include:

- Mechanistic studies: elucidating the interplay of glial cells, neuroinflammation, and vascular dynamics in delta rhythm generation. Investigating the role of extracellular potassium accumulation in modulating delta activity may also be fruitful.
- Longitudinal studies: examining delta rhythm changes during recovery and their relationship to neural plasticity. Such studies could identify biomarkers predictive of long-term outcomes.
- Clinical trials: evaluating the efficacy of delta-modulating interventions in large patient cohorts. Trials should aim to stratify patients based on baseline EEG features to optimize therapeutic targeting.
- Technological innovations: developing portable, high-density EEG systems to facilitate real-time monitoring of delta activity in clinical settings.

Conclusion

Delta rhythms offer profound insights into the neural disruptions underlying DOC. Advances in understanding their mechanisms and clinical implications hold promise for improving patient outcomes. Future research should focus on bridging experimental findings with translational applications to harness the diagnostic and therapeutic potential of delta rhythms fully. Integrating delta rhythm analysis with multimodal approaches and personalized therapies will likely define the next frontier in DOC management.

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