ACE: amplitude coalition entropy

AE: approximate entropy

AEP: auditory evoked potential

AUROC: area under the receiver operator characteristic curve

BS: burst suppression

LZC: Lempel-Ziv complexity

PCI: perturbational complexity index

PCMI: permutation cross-mutual information

PE: permutation entropy

PK/PD: pharmacokinetic/pharmacodynamic

Pk: prediction probability

BIS: Bispectral index

DFA: detrended fluctuation analysis

SCE: synchrony coalition entropy

SE: Sample entropy

SEF50: median frequency

SEF95: spectral edge frequency 95

TE: transfer entropy

TMS: transcranial magnetic stimulation

SVD: singular value decomposition

OAA/S: observer’s assessment of alertness/sedation score

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| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **No.** | **Study** | **Type** | **Measure** | **Method** | **Drugs** | **Subjects** | **Behavioral measure** | **Results** |
| 1 | (Watt and Hameroff, 1988) | temporal | phase space trajectories and dimensionality | EEG, broadband | isoflurane + fentanyl + thiopental | 1 surgical patient |  | discrimination of awake, anesthetized, and burst suppression |
| 2 | (Widman et al., 2000) | temporal | phase space based nonlinear correlation index | EEG, broadband | sevoflurane | surgical patients |  | superiority over spectral measures in the correlation with the effect-site concentration estimated via PK/PD model |
| 3 | (Bruhn et al., 2000a) | temporal | AE | EEG, broadband | desflurane | surgical patients |  | the performance as an indicator for desflurane concentrations was similar to SEF95 and BIS, and better than SEF50 (PK/PD modeling and Pk analysis) |
| 4 | (Bruhn et al., 2000b) | temporal | AE | EEG, broadband | isoflurane | surgical patients |  | AE, but not SEF50 or SEF95 without BS compensation, correctly classified the occurrence of BS as an increasing anesthetic drug effect (PK/PD modeling and correlation analysis) |
| 5 | (Zhang et al., 2001) | temporal | LZC | EEG, broadband | sevoflurane, isoflurane, propofol, or desflurane | surgical patients | responsiveness component of OAA/S scale | superiority over AE, spectral entropy and SEF50 in discriminating awake  and asleep states (sensitivity, specificity, and accuracy) |
| 6 | (Muncaster et al., 2003) | temporal | SVD entropy | EEG, broadband | sevoflurane + remifentanil | surgical patients | responsiveness to verbal commands,  OAA/S | SVD entropy, but not most of the EEG/AEP variables, was sensitive to the decrease in both anesthetics and the recovery of consciousness (Pk analysis) |
| 7 | (Vakkuri et al., 2004) | temporal | time-frequency balanced spectral entropy | EEG | propofol, sevoflurane, or thiopental | surgical patients | follow verbal commands | superior performance over BIS in distinguishing BS and indicating emergence from anesthesia (sensitivity, specificity, and Pk analysis) |
| 8 | (Sleigh et al., 2004) | temporal | spectral entropy | ECoG | propofol | sheep |  | spectral entropy could be a sensitive monitor of the consciousness-unconsciousness transition, rather than a progressive indicator of anesthetic drug effect |
| 9 | (Walling and Hicks, 2006) | temporal | chaos and correlation dimension | EEG, broadband | sevoflurane | surgical patients | follow verbal commands | demonstration of four dynamical stages during emergence from anesthesia - a classic route toward chaos |
| 10 | (Ferenets et al., 2007) | temporal | Higuchi fractal dimension, spectral entropy, AE, PE, LZC | EEG, broadbands with different sets of cutoff frequencies | propofol + remifentanil | surgical patients | OAA/S | cutting off high frequencies of EEG and increased remifentanil concentration deteriorated the performance of the entropy/complexity measures as indicators of the depth of propofol sedation (PK/PD modeling and Pk analysis) |
| 11 | (Jospin et al., 2007) | temporal | DFA | EEG, broadband | propofol | surgical patients |  | the proposed indexes allowed significant discrimination between awake, sedated and anesthetized states and presented a good correlation with established indexes of depth |
| 12 | (Olofsen et al., 2008) | temporal | composite PE index | EEG, broadband | sevoflurane or propofol | surgical patients | response to verbal commands | comparable performance with BIS and M-entropy indices (PK/PD modeling) |
| 13 | (Jordan et al., 2008) | temporal | AE, PE, RQA | EEG, broadbands with different settings for the high cutoff frequency | sevoflurane or propofol | surgical patients | follow  commands | nonlinear measures separated consciousness from unconsciousness and were grossly independent of high-frequency components of EEG (Pk analysis) |
| 14 | (Li et al., 2008a) | temporal | PE, AE | EEG, broadband | sevoflurane | surgical patients | response to verbal commands | PE estimated the sevoflurane drug effect more effectively than AE (PK/PD modeling and Pk analysis) |
| 15 | (Li et al., 2008b) | temporal | Hilbert-Huang spectral entropy | EEG | sevoflurane | surgical patients | response to verbal commands | the measure had a slightly stronger ability to track changes in sevoflurane effect-site concentration than M-Entropy with a stronger noise-resistance (PK/PD modeling and Pk analysis) |
| 16 | (Li et al., 2010) | temporal | multiscale PE | EEG, broadband | sevoflurane | surgical patients | response to verbal commands | multiscale PE outperformed the raw single-scale PE in reflecting the sevoflurane drug effect (PK/PD modeling and Pk analysis) |
| 17 | (Kekovic et al., 2010) | temporal | spectral entropy, Higuchi fractal dimension | ECoG/LFP, broadband | nembutal, ketamine or zoletil | rats | spontaneous foot movements and steady breathing rate | the measures were successfully used to describe not only cerebral activity but also the cerebellar activity in various states of consciousness |
| 18 | (Kaskinoro et al., 2011) | temporal | spectral entropy | EEG | dexmedetomidine, propofol, or sevoflurane | healthy volunteers | response to the request of opening eyes | because of wide inter-individual variability, BIS and entropy were not able to reliably differentiate consciousness from unconsciousness during and after stepwise increasing concentrations (Pk analysis) |
| 19 | (Silva et al., 2011) | temporal | PE, multiscale PE with BS correction | EEG | propofol | rabbits | postural reflex, muscular tone, palpebral reflex, corneal reflex, laryngeal reflex, ear pinch, and digital (pedal) reflexes | PE with BS correction showed better performance than other EEG-derived parameters but not better than the electromyographic activity (PK/PD modeling and Pk analysis) |
| 20 | (Shalbaf et al., 2012) | temporal | SE | EEG, broadband | sevoflurane | surgical patients | response to verbal commands | SE estimated the sevoflurane drug effect on the EEG more effectively than the index in M-module with a stronger noise resistance (PK/PD modeling and Pk analysis) |
| 21 | (Liang et al., 2012) | temporal | multiscale hurst exponent | EEG, broadband | sevoflurane | surgical patients | response to verbal commands | superiority over single-scale measure in tracking drug effect (PK/PD modeling and Pk analysis) |
| 22 | (Liang et al., 2013) | temporal | permutation auto-mutual information | EEG, broadband | sevoflurane | surgical patients | response to verbal commands | superiority over traditional auto-mutual information and other measures (PK/PD modeling and Pk analysis) |
| 23 | (Schneider et al., 2014) | temporal | multimodal index derived from multi-parameters including AE and PE | EEG, broadband, data-driven approach | 10 different anesthetic regimens | 263 surgical patients | response to a repeated verbal command | the multimodal index showed significant higher Pk value to separate different levels of anesthesia (wakefulness to burst suppression) as compared to BIS |
| 24 | (Wang et al., 2014) | temporal | multiscale SE | EEG, broadband | sevoflurane | surgical patients | response to verbal commands | superiority over AE and spectral entropy in tracking drug concentration change (PK/PD modeling and Pk analysis) |
| 25 | (Maciver and Bland, 2014) | temporal | chaotic attractor shape | EEG | isoflurane | rats | righting reflex, paw pinch and tail clamp responses | the measure was better in discerning between EEG activations at loss of responses than spectral analysis; it changed gradually through the transition from awake to loss of righting reflex, indicating a point along a continuum of brain states but not an on/off like transition |
| 26 | (Liang et al., 2015a) | temporal | 12 entropy measures | EEG, broadband | sevoflurane or isoflurane | surgical patients | response to verbal commands | each measure had its advantages and disadvantages in estimating depth of anesthesia; Renyi PE showed overall superior performance (PK/PD modeling and Pk analysis) |
| 27 | (Bai et al., 2015) | temporal | permutation LZC | EEG,  broadband | sevoflurane or propofol | surgical patients or healthy volunteers | response to verbal commands or  syringe-drop time | superiority over conventional LZC, PE and parameters in BIS and M-module (PK/PD modeling and Pk analysis) |
| 28 | (Krzeminski et al., 2017) | temporal | DFA | ECoG, frequency bands of delta, alpha, beta, ow- and high-gamma | ketamine + medetomidine, ketamine, medetomidine, or propofol | macaque monkeys | responsive to manipulation of a hand or touching nostrils | general anesthesia affected mainly brain areas characterized by strongest long-range temporal correlations during wakefulness |
| 29 | (Wang et al., 2017) | temporal | mean information gain and fluctuation complexity | EEG, broadband | ketamine, propofol | surgical patients or healthy volunteers | response to verbal commands | both ketamine and propofol reduced the complexity, but ketamine increased the randomness and propofol decreased it |
| 30 | (Eagleman et al., 2018a) | temporal | phase-space geometric characterization of time-delayed embeddings | EEG, broadband | remifentanil + nitrous oxide | surgical patients | response to verbal stimuli | the proposed nonlinear measure showed more significant differences between states than most spectral measures |
| 31 | (Eagleman et al., 2018b) | temporal | correlation dimension, ellipse radius ratio, and multiscale SE | EEG, broadband | fentanyl+ propofol | geriatric patients | response to verbal stimuli | the proposed measure showed significant differences before and after loss of response, as did measure of multiscale SE |
| 32 | (Thiery et al., 2018) | temporal | DFA | EEG, frequency bands from delta to gamma | sevoflurane | healthy volunteers | response to verbal commands | unconsciousness was associated with increases in long-range temporal correlations in beta amplitude over frontocentral channels and with a suppression of alpha amplitude over occipitoparietal electrodes; the combination of both bands provided the highest classification accuracy to predict states of consciousness |
| 33 | (Timmermann et al., 2019) | temporal | LZC, spectral exponent | EEG, broadband | DMT | healthy volunteers | micro-phenomenological interview | DMT robustly increased spontaneous signal diversity that parallel broad and specific components of the subjective experience |
| 34 | (Colombo et al., 2019) | temporal | spectral exponent | EEG, broad bands (1-40 Hz) and narrower sub-bands (1-20 Hz, 20-40 Hz) | propofol, xenon, or ketamine | healthy volunteers | Ramsay score, retrospective reports | the spectral exponent was highly correlated to PCI, and could discriminate states in which consciousness was present from states where consciousness was reduced or abolished (linear discriminant analysis and accuracy, sensitivity, specificity, and AUROC) |
| 35 | (Ramaswamy et al., 2019) | temporal | 44 measures including SVD entropy, spectral entropy, SE, Rényi entropy, Shannon entropy, PE, and fractal dimension | EEG, machine learning | propofol, sevoflurane, or dexmedetomidine | 102 healthy volunteers | modified OAA/S score | different features were selected for propofol, sevoflurane, and dexmedetomidine groups, but the sedation-level estimator maintained a high performance for predicting modified OAA/S score independent of the drug used (AUROC) |
| 36 | (Kreuzer et al., 2020) | temporal | AE, PE  spectral 1/f slope | EEG, broadband and alpha, beta bands | sevoflurane | 180 surgical patients | clinical level of general anesthesia without surgical stimulation | older age was associated with a shift to a less predictable EEG (regression analysis and AUROC) |
| 37 | (Brito et al., 2020) | temporal | LZC | EEG, broadbands | ketamine or propofol | rats | righting reflex | ketamine anesthesia was characterized by reduced complexity in high gamma bandwidth, as reflected in both raw and phase shuffled normalized LZC |
| 38 | (Boncompte et al., 2021) | temporal | LZC | EEG, broadband and frequency bands from delta to gamma | propofol | healthy volunteers | response to an auditory discrimination task | complexity increased in response to propofol, particularly during low-dose sedation, which was independent of frequency-specific spectral power manipulations, and most prominent in frontal areas |
| 39 | (Vrijdag et al., 2021) | temporal | RQA | EEG, broadband | low-dose nitrous oxide | healthy volunteers | Psychometric tests | temporal complexity decreased most markedly in medial cortical regions, and this change tracked psychometric impairment (linear mixed-effects model, AUROC) |
| 40 | (Chen et al., 2021) | temporal | variability | EEG, broadband | sevoflurane, desflurane or propofol | surgical patients | expert  assessments of conscious level | the proposed measure surpassed PE, AE, SEF50 and SEF95 in detection accuracy of unconscious state and tracking the level of consciousness (AUROC and Pearson correlation coefficient) |
| 41 | (Hudetz, 2002) | temporal (2 channels) | cross AE | epidural EEG, broadbands | isoflurane or halothane | rats | righting reflex | cross-AE of bi-hemispheric EEG was a sensitive, agent-specific correlate of anesthetics’ central effect |
| 42 | (Imas et al., 2005) | temporal (2 channels) | transfer entropy | light flash-evoked EEG | halothane or isoflurane | rats | righting reflex | inhalational anesthetics preferentially impaired frontal-posterior feedback information transfer at high gamma frequencies |
| 43 | (Kreuzer et al., 2010) | temporal (2 channels) | cross AE | LFP | Isoflurane, enflurane, or halothane | rats |  | cortical LFP signals in the somatosensory cortex were more synchronous in the presence of anesthetics |
| 44 | (Ku et al., 2011) | temporal (2 channels) | symbolic TE | EEG, broadband | propofol or sevoflurane | surgical patients | response to verbal commands | the disruption of dominant feedback connectivity in the frontoparietal network was a common neurophysiologic correlate of general anesthesia induced by propofol and sevoflurane |
| 45 | (Lee et al., 2013b) | temporal (2 channels) | symbolic TE | EEG, broadband, multiscale | ketamine, propofol, or sevoflurane | surgical patients | response to verbal commands | ketamine, propofol, and sevoflurane all selectively impaired frontal-to-parietal brain communication |
| 46 | (Jordan et al., 2013) | temporal (2 channels),  temporal | symbolic TE, PE | EEG, broadband | propofol | healthy volunteers | response to verbal commands | the changes of directional connectivity in frontal-parietal and frontal–occipital correlated with functional connectivity changes in fMRI analysis |
| 47 | (Untergehrer et al., 2014) | temporal (2 channels) | symbolic TE | EEG, broadband | propofol | healthy volunteers | following commands | the fronto-parietal connectivity was a non-static phenomenon, in terms of intensity and transfer time |
| 48 | (Liang et al., 2015b) | temporal (2 channels) | PCMI | EEG, broadband | remifentanil +isoflurane | surgical patients | response to verbal commands | PCMI could track the effect of anesthesia and distinguish the consciousness state from the unconsciousness state |
| 49 | (Shalbaf et al., 2015) | temporal (2 channels) | cross RQA | EEG, broadband | propofol | healthy volunteers | syringe-drop time; respond to verbal commands | the proposed index could estimate anesthetic state of patient more efficiently than the BIS index in lightly sedated state with more tolerant of artifacts (PK/PD modeling and Pk analysis) |
| 50 | (Pal et al., 2016) | temporal (2 channels) | symbolic TE | EEG, frequency bands of theta, low-, medium-, and high-gamma | propofol or sevoflurane | rats | righting reflex | frontal–parietal connectivity in high gamma bandwidth correlated with behavioral arousal and was not mediated by cholinergic mechanisms, while theta connectivity correlated with cortical acetylcholine levels |
| 51 | (Ranft et al., 2016) | temporal (2 channels),  temporal | symbolic TE, PE | EEG, broadband | sevoflurane | healthy volunteers | response to verbal commands | EEG analysis showed a significant reduction of anterior-to-posterior symbolic TE and global PE, consistent with changes in fMRI functional connectivity analysis |
| 52 | (Liang et al., 2016) | temporal (2 channels) | Multiple measures including PCMI, cross RQA, etc. | EEG | propofol | healthy volunteers | syringe-drop time; respond to verbal commands | nonlinear measures correlated closely with each other and had a better robustness to noise and higher correlation with BIS and drug concentration than other synchronization indexes (PK/PD modeling and Pk) |
| 53 | (Wollstadt et al., 2017) | temporal (2 channels),  temporal | TE, active information storage, differential entropy | LFP | isoflurane | ferrets | righting reflex | changes in information transfer under isoflurane seemed to be a consequence of changes in local processing more than of decoupling between brain areas |
| 54 | (Lee et al., 2017a) | temporal (2 channels) | phase lag entropy | EEG, broadband (8-30 Hz) | propofol | healthy volunteers or surgical patients | response to verbal commands or MOAA/S | the dynamics of the phase relationship between frontal channels became progressively less diverse and more stereotyped during unconsciousness; the proposed measure showed the highest agreement with the level of consciousness, compared to measures including AE and PE (AUROC, Pk analysis) |
| 55 | (Afshani et al., 2019) | temporal (2 channels) | standardized permutation mutual information | EEG, broadband | propofol | healthy volunteers | syringe-drop time; respond to verbal commands | the proposed index had higher correlation with estimated effect-site concentration and better ability to distinguish three anesthetic states than the other connectivity indexes and the BIS index (PK/PD modeling and Pk analysis) |
| 56 | (Yang et al., 2019) | temporal (2 channels), temporal | AE, cross AE | LFP, broadband | propofol | rats | touch reflex, reversal reflex or tail-pinch reflex | the cortex rather than the subcortical structures, and the cortex-subcortical connectivity instead of subcortical connectivity could be the more vulnerable targets of propofol during anesthesia |
| 57 | (Zhao et al., 2021) | temporal (2 channels) | symbolic TE | EEG, source space | propofol | healthy volunteers |  | the disconnection of frontal-parietal connectivity was a signature of propofol-induced anesthesia, and this did not depend on the analytical method |
| 58 | (Sanjari et al., 2021) | temporal (2 channels) | TE | EEG, broadband | propofol | healthy volunteers | syringe-drop time; response to verbal commands | TE could effectively follow the effect-site concentration and distinguish the anesthetic states, and performed better than the other effective connectivity indexes and BIS index (PK/PD modeling and Pk analysis) |
| 59 | (Cimenser et al., 2011) | spatial | ratio of the largest eigenvalue to the sum of all eigenvalues | EEG, cross-spectrum, delta and alpha | propofol | healthy volunteers | response to an auditory binary choice task | it showed strong coordinated alpha activity in the occipital leads in the awake state that shifted to the frontal leads during unconsciousness and revealed a lack of coordinated delta activity during both the awake and unconscious states |
| 60 | (Lee et al., 2011) | spatial | global efficiency | EEG, broadband,  cross correlation | propofol | healthy volunteers | response to commands | loss of consciousness was consistently associated with a disruption of network topology; both continuous and discrete elements were observed in transitions between the awake and anesthetized states, particularly in the parietal cortex |
| 61 | (Kuhlmann et al., 2013) | spatial | global efficiency, ratio of the largest eigenvalue to the sum of all eigenvalues | EEG, cross correlation, cross-spectrum | nitrous oxide | healthy volunteers | response to an auditory continuous performance task | nitrous oxide reduced functional connectivity in the scalp EEG most strongly in the parietal area and induced spatially coherent and widespread perturbations in frontal activity (AUROC) |
| 62 | (Lee et al., 2013a) | spatial | graph theoretical measures | EEG, frequency bands from delta to beta, phase lag index | propofol | healthy volunteers | response to verbal commands | topology rather than connection strength of functional networks correlated with states of consciousness |
| 63 | (Li et al., 2013) | spatial | entropy of the eigenvalues | ECoG, frequency bands from beta to gamma, coherence | sevoflurane, desflurane, isoflurane, or enflurane | sheep |  | over a local spatial scale of 2–14 mm, synchrony increased during general anesthesia, correlated with anesthetic-induced cortical depression (Pk analysis) |
| 64 | (Martin et al., 2014) | spatial | global efficiency, ratio of the largest eigenvalue to the sum of all eigenvalues | EEG,  cross-correlation, cross-spectrum | sevoflurane | surgical patients (children) | clinical behavior assessment for delirium | increased frontal lobe cortical functional connectivity was observed in patients with emergence delirium, immediately after the termination of sevoflurane anesthesia |
| 65 | (Chennu et al., 2016) | spatial | graph theoretical measures | EEG, alpha band, weighted phase lag index | propofol | healthy volunteers | response to an auditory discrimination task | participants who had weaker alpha band networks at baseline were more likely to become unresponsive during sedation, despite similar levels of drug in blood |
| 66 | (Numan et al., 2017) | spatial | minimum spanning tree measures | EEG, frequency bands from delta to beta, phase lag index, directed phase transfer entropy | sevoflurane or isoflurane | surgical patients | clinical assessment for delirium | in hypoactive delirium there was a less integrated network in the alpha band; during recovery from anesthesia there was increased integration in the delta band |
| 67 | (Blain-Moraes et al., 2017) | spatial | global efficiency and other graph theoretical measures | EEG, alpha wPLI | propofol + isoflurane | healthy volunteers | response to verbal commands | network efficiency was significantly depressed and network clustering coefficient was significantly increased during unconsciousness |
| 68 | (Lee et al., 2017b) | spatial | graph theoretical measures | EEG, frequency bands from delta to beta, weighted phase lag index | propofol | healthy volunteers | response to auditory stimuli | global and local efficiencies in the delta band were significantly increased during transition into unconsciousness |
| 69 | (Kim et al., 2018b) | spatial | average node degree, topographical similarity | EEG, alpha band, phase lag index | sevoflurane or ketamine | healthy volunteers | response to verbal commands | the structure and strength of functional brain networks reconfigured differently during the loss vs. recovery of consciousness |
| 70 | (Pappas et al., 2019) | spatial | degree entropy and modularity | EEG, delta band, both sensor and source level,  imaginary coherence | sevoflurane | surgical patients (infants) |  | in infants, slow-wave functional connectivity broke down during general anesthesia and brain networks were less integrated |
| 71 | (Liang et al., 2020) | spatial | graph theoretical measures | ECoG, broadband,  genuine PCMI | propofol | epilepsy patients | response to verbal commands | with loss of consciousness, there was a loss of efficient global information transmission and increased local functional segregation in the cortical network |
| 72 | (Lee et al., 2020) | spatial | graph theoretical measures | EEG, frequency bands from delta to gamma, lagged phase coherence | nitrous oxide | healthy volunteers | responses to verbal commands | nitrous oxide interfered with the efficiency of information integration in the frequency bands important for cognitive processes and attention task |
| 73 | (Bi et al., 2021) | spatial | graph theoretical measures | EEG, frequency bands from delta to gamma, sparse representation | propofol, sevoflurane or ketamine | surgical patients | response to trapezius squeeze | network measures based on sparse representation method had better performance in distinguishing anesthetic-induced loss of consciousness from awake state than traditional coherence analysis |
| 74 | (Li et al., 2021b) | spatial | graph theoretical measures | EEG, alpha band, coherence | propofol + sevoflurane | surgical patients | spontaneous movement, response to any stimulus, eyelash reflex, and response to verbal commands | using related network parameters to recognize the loss of consciousness from the resting state, the fused network topologies and properties achieved the best performance (accuracy, sensitivity, specificity) |
| 75 | (Li et al., 2021a) | spatial | graph theoretical measures | EEG, alpha band, cross-fuzzy entropy | propofol + sevoflurane | surgical patients | spontaneous movement, response to any stimulus, eyelash reflex, and response to verbal commands | the time-varying cross-fuzzy networks could help decode the general anesthesia |
| 76 | (Lee et al., 2009) | spatiotemporal | mean information integration capacity | EEG, broadband and narrow bands from delta to gamma, state space reconstruction and SVD | propofol | surgical patients | response to verbal commands | induction of general anesthesia with propofol reduced the capacity for information integration in the brain, most prominently in gamma band |
| 77 | (Lee et al., 2010) | spatiotemporal | connection entropy | EEG, broadband and narrow bands from delta to gamma,  Pearson correlation | propofol | healthy volunteers | response to verbal commands | general anesthesia was associated with a significant reduction in the number of network connections and entropy of the connection matrix, while a fundamental principle of temporal organization of network connectivity was maintained during consciousness and anesthesia |
| 78 | (Ferrarelli et al., 2010) | spatiotemporal | significant current scattering | TMS-EEG | midazolam | healthy volunteers | OAA/S | the measure of the propagation of evoked cortical currents could reliably discriminate between consciousness and loss of consciousness |
| 79 | (Casali et al., 2013) | spatiotemporal | PCI | TMS-EEG | midazolam, xenon, or propofol | healthy volunteers | modified OAA/S | PCI reliably discriminated the level of consciousness in single individuals during wakefulness and anesthesia |
| 80 | (Alonso et al., 2014) | spatiotemporal | stability | ECoG, broadband, eigenmode decomposition of the autoregressive matrices | propofol | epilepsy patients | respond to verbal commands | as the subject becomes anesthetized, significant increase was observed in the stability of neuronal dynamics, most prominently for high frequency oscillations; stabilization was not observed in phase randomized surrogate data |
| 81 | (Solovey et al., 2015) | spatiotemporal | stability | ECoG, broadband, eigenmode decomposition of the autoregressive matrices | ketamine and medetomidine, or propofol | macaque monkeys | responsive to manipulation of a hand or touching nostrils | stability could be an emergent phenomenon dependent on the correlations among activity in different cortical regions rather than signals taken in isolation |
| 82 | (Sarasso et al., 2015) | spatiotemporal | PCI | TMS-EEG | propofol, xenon, or ketamine | healthy volunteers | Ramsay scale score, retrospective reports | PCI in propofol and xenon anesthesia was low, while ketamine was associated with high PCI and by vivid post-anesthesia dream reports |
| 83 | (Schartner et al., 2015) | spatiotemporal | LZC, ACE, SCE | EEG, broadband and narrow bands from delta to gamma | propofol | healthy volunteers | response to commands, Ramsay scale score | there was a robustly measurable decrease in the complexity of spontaneous EEG during general anesthesia (AUROC) |
| 84 | (Hudetz et al., 2016) | spatiotemporal | repertoire of mesoscopic brain states | LFP | desflurane | rats |  | the repertoire of population activity and self-organized criticality at the mesoscopic scale did not appear to contribute to anesthetic suppression of consciousness |
| 85 | (Schartner et al., 2017) | spatiotemporal; temporal | LZC, ACE, SCE | MEG, broadband | ketamine, LSD or psilocybin | healthy volunteers | questionnaire scores | the sustained occurrence of psychedelic phenomenology constituted an elevated level of consciousness as measured by neural signal diversity |
| 86 | (Kim et al., 2018a) | spatiotemporal | integrated information | EEG, frequency bands from delta to gamma | ketamine or propofol+ isoflurane | healthy volunteers | response to verbal commands | the proposed method was insufficient to discriminate certain states of anesthesia, while a multi-dimensional parameter space supplemented by EEG connectivity was able to differentiate all states of consciousness |
| 87 | (Kim and Lee, 2019) | spatiotemporal | integrated information, pair correlation function | EEG, alpha | sevoflurane | healthy volunteers | response to verbal commands | the conscious resting state showed the largest values in integrated information measure and criticality, whereas the balance between variation and constraint in the brain network broke down as the response rate dwindled |
| 88 | (Lee et al., 2019) | spatiotemporal;  spatial | pair correlation function,  topographical similarity | EEG, broadband (2-25 Hz), phase lag entropy | ketamine or propofol+ isoflurane | healthy volunteers | response to the verbal commands | the partial phase locking at criticality shaped the functional connectivity and asymmetric anterior-posterior phase lag entropy topography; the topographical similarity and the strength of phase lag entropy differentiated various pharmacologic and pathologic states of consciousness |
| 89 | (Wenzel et al., 2019) | spatiotemporal | repertoire of microstates/ neuronal ensembles | LFP and two-photon calcium imaging in mice  SUA and LFP in humans,  t-SNE/watershed segmentation, affinity propagation clustering, PCA, and Lempel-Ziv-Welch complexity | isoflurane, propofol | mice, epilepsy patients | clinical parameters (breath rate and reaction to tail pinching) and locomotion | medically induced loss of consciousness disrupted population activity patterns by generating fewer discriminable network microstates and fewer neuronal ensembles |
| 90 | (Comolatti et al., 2019) | spatiotemporal | PCI state-transition (PCIST) | TMS-EEG | midazolam, xenon, or propofol | healthy volunteers |  | PCIST could be a fundamental advancement towards the implementation of a reliable and fast clinical tool for the bedside assessment of consciousness |
| 91 | (Li and Mashour, 2019) | spatiotemporal | LZC | EEG, broadband | ketamine | healthy volunteers | response to verbal commands | spatiotemporal complexity associated with ketamine-induced state transitions had features of general anesthesia, normal consciousness, and altered states of consciousness |
| 92 | (Varley et al., 2020) | spatiotemporal | avalanche dynamics and complexity | ECoG, broadband | ketamine or propofol | macaque monkeys | response to manipulation of a hand or touching nostrils | propofol restricted the size and duration of avalanches and triggered a large reduction in the complexity of brain dynamics, while ketamine allowed for more awake-like dynamics to persist; all states, however, showed some signs of persistent criticality |
| 93 | (Farnes et al., 2020) | spatiotemporal | LZC, ACE, SCE  PCI | EEG, broadband | ketamine | healthy volunteers | psychedelic assessment | although no significant difference was found in TMS-evoked complexity, all measures of spontaneous EEG signal diversity showed significantly increased values in the sub-anesthetic ketamine condition; this increase correlated with subjective assessment of altered states of consciousness |
| 94 | (Afrasiabi et al., 2021) | spatiotemporal | integrated information | LFP, broadband, machine learning | propofol or isoflurane | macaques | limb/face movements, oral signs, body movements, eye movements, vital signs | the measure of neural integration robustly correlated with changes in consciousness; machine learning approaches showed parietal cortex, striatum, and thalamus contributed more than frontal cortex to decoding differences in consciousness (accuracy and F-score) |
| 95 | (Dasilva et al., 2021) | spatiotemporal; spatial | wave propagation entropy (diversity of slow wave propagation patterns);  functional complexity; PCI | LFP/MUA, spontaneous and electrical stimulation, cross correlation | isoflurane | mice | righting reflex | cortical complexity could vary within a single brain state dominated by slow oscillations: both perturbational and spontaneous complexity increased with decreasing anesthesia levels, which were related to, but not dependent on, changes in excitability |
| 96 | (Varley et al., 2021) | spatiotemporal, temporal | multi-channel: topological analysis  single-channel: information-theoretic measures of ordinal partition network | ECoG, broad band | ketamine or propofol | macaque monkeys | response to manipulation of a hand or touching nostrils | the awake condition had the ‘richest’ structure, visiting the most states, the presence of pronounced higher-order structures, and the least deterministic dynamics; the propofol condition had the most dissimilar dynamics, transitioning to a more impoverished, constrained, low-structure regime; the ketamine condition seemed to combine aspects of both |
| 97 | (Arena et al., 2021) | spatiotemporal | PCIST | EEG, intracranial electrical stimulation | propofol, sevoflurane, or ketamine | rats | righting reflex, reactions to pain stimulations, whisker tracking | PCI correlated with functional connectivity and pattern diversity, and collapsed from wakefulness to general anesthesia; brief periods of activity-dependent neuronal silence could interrupt complex interactions in neocortical circuits |
| 98 | (Puglia et al., 2021) | spatiotemporal; temporal | LZC | EEG, broadband | combined anesthetic agents in common clinical use | surgical patients (children) | University of Michigan Sedation Scale | cortical complexity increased with developmental age and decreased during general anesthesia; this association remained significant when controlling for spectral changes during anesthetic-induced perturbations in consciousness but not with developmental age |
| 99 | (Artoni et al., 2021) | spatiotemporal | LZC of microstate sequences | EEG, broadband, microstate analysis | propofol | surgical patients | modified OAA/S | it showed an initial increase in microstates’ temporal dynamics and complexity with increasing depth of sedation leading to a distinctive “U-shape” |

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