



CLINICAL REVIEW

From state dissociation to status dissociatus



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SUMMARY

The states of being are conventionally defined by the simultaneous occurrence of behavioral, neurophysiological and autonomic descriptors. State dissociation disorders are due to the intrusion of features typical of a different state into an ongoing state. Disorders related to these conditions are classified according to the ongoing main state and comprise: 1) Dissociation from prevailing wakefulness as seen in hypnagogic or hypnopompic hallucinations, automatic behaviors, sleep drunkenness, cataplexy and sleep paralysis 2) Dissociation from rapid eye movement (REM) sleep as seen in REM sleep behavior disorder and lucid dreaming and 3) Dissociation from NREM sleep as seen in the disorders of arousal.

The extreme expression of states dissociation is characterized by the asynchronous occurrence of the various components of the different states that prevents the recognition of any state of being. This condition has been named *status dissociatus*. According to the underlying disorders/diseases and to their severity, among *status dissociatus* we may recognize disorders in which such an extreme dissociation occurs only at night time or intermittently (i.e., autoimmune encephalopathies, narcolepsy type 1 and IgLON5 parasomnia), and others in which it occurs nearly continuously with complete loss of any conventionally defined state of being, and of the circadian pattern (*agrypnia excitata*).

Here, we render a comprehensive review of all diseases/disorders associated with state dissociation and *status dissociatus* and propose a critical classification of this complex scenario.

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Introduction

The states of being are characterized by an identifiable and stable cluster of behavioral, neurophysiological and autonomic descriptors, observed over a period of time. In the classical sleep stage scoring system [1], this period has an arbitrary fixed length of 30 s, allowing the identification of both long-lasting phenomena, such as muscle tone changes, subcontinuous EEG alpha or slow-

wave activity, eye closure, immobility/activity, etc., and short-lasting transient phenomena such as eye movements, short muscle contractions, sleep spindles, K-complexes, etc. The combination of these parameters has empirically allowed finding clusters defining each state (namely wakefulness, rapid eye movement (REM) sleep and NREM sleep) (Supplemental materials: Table 1).

These clusters are typically preserved in most of the sleep disorders (e.g., insomnia, sleep-related breathing disorders, circadian disorders) and eventual changes involve their quantity, rather than their basic features. However, a particular group of other conditions is characterized by the disintegration of these clusters, with the asynchronous occurrence of the various components of the different states that prevent the recognition of a well-defined

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Abbreviations	
AMBEs	arousal-related motor-behavioral episodes
caspr2	contactin-associated protein 2
CSF	cerebro-spinal fluid
DLB	dementia with lewy bodies
EEG	electroencephalography
EMG	electromyography
FFI	Fatal familial insomnia
GBS	Guillain Barré syndrome
Hcrt	hypocretin
Lgi1	leucine-rich glioma inactivated 1
MSA	multiple system atrophy
NMDA	N-methyl-D-aspartate
N type 1	narcolepsy type 1
OSAS	obstructive sleep apneas during sleep
PD	Parkinson disease
PLMs	periodic leg movements
POD	parasomnia overlap disorder
PSG	polysomnography
RBD	REM sleep behavior disorder
REM	rapid eyes movement
RWA	REM-sleep without atonia
SD	status dissociatus
SOREMP	REM sleep onset periods
VGKC-Ab	voltage-gated potassium channel complex antibodies
W	wake

cluster defining a single state over the established epoch length [2,3]. This group of conditions will be the focus of this review.

It is important to pinpoint that also in normal subjects an admixture of features of different stages may occur, mainly at state transition. Usually, this dissociation is brief and emerges only at a neurophysiological level; however, if it lasts longer, it may result in behaviors such as hypnagogic hallucinations, lucid dreams or sleep paralysis.

For the sake of clarity, it should also be mentioned here that the type of sleep abnormalities that will be discussed in this review does not always refer to the recently introduced concept of “local sleep” [4]. This concept refers to the possibility to identify discrete neuronal aggregates that show features of one state while others are exhibiting features of a different state also in physiological sleep of healthy controls. However, the sleep/wake dynamics are still recognizable as a “global” phenomenon during which “local” neuronal aggregates might disentangle temporarily from the global state and engage a different state, obtaining a sort of state dissociation. On the contrary, the conditions that will be mainly treated here can be characterized by a much more stable and profound dissociation during which no feature clusters nor states can be distinguished. However, in order to give a comprehensive analysis of the topic, on some occasion we will present also milder conditions that might be explained by an extension to pathology of the concept of “local sleep” mechanisms.

Literature search criteria

We searched the Medline database (via PubMed: <http://www.ncbi.nlm.nih.gov>) for publication between 1986 to January 2015, using the search terms: *status dissociatus* (SD), state dissociation, dissociation of states, dissociated states, narcolepsy, narcolepsy with cataplexy, narcolepsy type 1, REM sleep behavior disorders, parasomnia, parasomnia-overlap syndrome, lucid dreaming, hallucinations, sleep inertia, sleep paralysis, *agrypnia excitata*, polysomnography* and encephalopathies, drug intoxications, alcohol withdrawal, neurodegenerative diseases. Only papers in English were selected and reference lists of the articles retrieved by the electronic searches were checked for other relevant reports not indexed in the electronic database. In addition, original articles focusing on pathophysiology, or single case reports of particular interest were eventually included even if published before 1986.

From dissociation of states to “*status dissociatus*”

In 1991, Mahowald and Schenck [2] proposed a classification of the dissociation of states based on the parent (or main) state; by using this model, the following dissociations can be recognized:

- Dissociation from prevailing wakefulness, due to intrusion of features of other stages into ongoing wakefulness;
- Dissociation from NREM sleep, due to intrusion of features of other stages into ongoing NREM sleep and;
- Dissociation from REM sleep, due to intrusion of features of other stages into ongoing REM sleep.

For the sake of simplicity, we will use the labels reported above to classify the spectrum of state dissociation disorders. The number of diseases, which can be associated with an abnormal dissociation of states is extensive (Supplemental materials: Table 2). However, one should acknowledge that the above-mentioned classification is not always thorough as there are more complex conditions (i.e., parasomnia overlap disorder) that would not fit in any of these boxes. Moreover, as for all the classifications, which try to underpin the complexity of human brain, this categorization may at times sound artificial as in particular conditions more than one type of dissociation may occur simultaneously. Examples are conditions classified among the “within-mind” dissociation that may present also with features of the “mind-body” dissociation (as seen in automatic behaviors or in NREM parasomnia) or vice-versa as seen in sleep paralysis (see later).

Dissociation from wakefulness

There are several examples of behaviors/disorders emerging from the intrusion of other states into wakefulness.

Within-mind dissociation

In this subtype of dissociation from wakefulness, the mind simultaneously contains elements of wake as subjects may retrieve quite a good recollection of the mental experience and of the environmental stimuli and a wake motor aspect (eyes open, motor tone present with at times even complex motor behaviors) and elements of REM sleep (vivid dreams) or of NREM sleep (dream-like mentation).

They include hypnagogic or hypnopompic hallucinations, and complex nocturnal hallucinations in which dream mentation occurs during the transition from sleep to wakefulness and vice versa. Hallucinations at the wake–sleep transition are typical of narcolepsy [5,6], although they can also be the consequence of alcohol/drug intoxication or withdrawal, of brainstem or thalamic lesions, severe visual loss (Charles Bonnet syndrome) and of other neurological conditions (autoimmune encephalitis) [5].

Yet, visual hallucinations are common in neurodegenerative diseases, such as Parkinson disease (PD) and dementia with Levy

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