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Behavioural and neurophysiological correlates of human cataplexy: A video-polygraphic study

Roberto Vetrugno [a,*], Roberto D'Angelo [a], Keivan Kaveh Moghadam [a], Stefano Vandi [a], Christian Franceschini [a], Emmanuel Mignot [b], Pasquale Montagna [a], Giuseppe Plazzi [a]

[a] Department of Neurological Sciences, University of Bologna, Bologna, Italy
[b] Stanford University Center for Narcolepsy, Palo Alto, CA, USA

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ABSTRACT

Objectives: To investigate the behavioural and neurophysiological pattern of cataplexy.
Methods: Seven narcolepsy with cataplexy patients underwent daytime videopolygraphy using humorous movies or/and jokes to trigger cataplectic attacks.
Results: During segmental cataplectic attacks, EMG showed brief and irregular periods of silencing focally involving facial, neck, axial or limb muscles, sometimes coinciding with bursts of rapid eye movements. All patients enacted intentional movements in response to these segmental postural lapses. During global cataplectic attacks, EMG showed suppression of activity alternated with patterned enhancement, enhanced EMG activity in neck muscles preceding that of other cranial, axial and lower limb muscles. This waxing and waning EMG pattern ended with a complete body collapse and persistent muscle atonia. Breathing irregularities, heart rate (HR) instability and EEG desynchronization were observed during global cataplectic attacks without any appreciable blood pressure changes, but with HR deceleration and silencing of sympathetic skin response while in complete atonia. Patients subjectively perceived the involuntary postural lapses as startling and alarming.
Conclusions: Cataplexy in our patients showed many of the features of tonic REM sleep.
Significance: Cataplexy can be construed as a "freezing-like" perturbation of the orienting response with transient impairment of posture and movements resulting in a "patchwork-compromise-behaviour".

1. Introduction

Cataplexy is best defined as a transient loss of muscle tone triggered by strong emotions and typically occurring while laughing or joking (Krahn et al., 2005). It is a core symptom of narcolepsy with cataplexy (NC), and is most often present at disease onset (Gélineau, 1880; Okun et al., 2002; American Academy of sleep Medicine, 2005). Although cataplexy can result in a dramatic and complete loss of postural muscle tone, resulting in a fall with complete paralysis, loss of tone is more often partial, affecting only some muscles. In these cases it may result in head nodding, limb weakness, slurred speech or facial muscle flickering. Facial attacks with tongue protrusion and closure of eyelids ("cataplectic facies"), are often found around disease onset, sometimes without any clear emotional precipitants (Plazzi et al., 2006, 2008; Serra et al., 2008). Generalized forms leading to falls are reported by 25% of NC patients (Bassetti and Aldrich, 1996; Sturzenegger and Bassetti, 2004).

Behavioural and polygraphic criteria for cataplexy have recently been suggested for a murine model of narcolepsy, in which cataplexy is obviously not emotionally triggered (Scammel et al., 2009). By contrast, polygraphic or video-polygraphic studies of cataplexy in human narcolepsy are few and have shown a complex mixture of suppression and enhancement of EMG activity in different muscular segments resulting in postural instability if not falls in some cases (Scollo-Lavizzari, 1970; Guilleminault, 1976; Rubboli et al., 2000; Donadio et al., 2008; Serra et al., 2008).

Cataplectic attacks may last from a few seconds to minutes, and their duration can be prolonged by emotional stimuli (i.e. by reiteration of the trigger, intervention of helpers). Attacks of long duration may evolve into a frank REM sleep episode. In rare cases, cataplectic spells may occur in tightly packed clusters, or be almost continuous, a condition known as "status cataplecticus". This particular condition may appear at the onset of the disease or may be provoked by antidepressant withdrawal (Plazzi et al., 2007; Serra

* Corresponding author. Address: Dipartimento di Scienze Neurologiche dell'Università di Bologna, Via Ugo Foscolo 7, 40123 Bologna, Italy. Tel.: +39 051 2092925; fax: +39 051 2092963.
E-mail address: roberto.vetrugno@unibo.it (R. Vetrugno).

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et al., 2008). Unfortunately, it is at risk of being mistaken for a psychogenic symptom (Simon et al., 2004).

Cataplexy has long been thought to represent the abnormal expression of REM sleep, whereby muscular atonia typical of REM sleep occurs inappropriately when awake (American Academy of Sleep Medicine, 2005). Some features of cataplexy, however, do not fully conform to this view (Tucci and Plazzi, 2009). This study is a video-polygraphic analysis of cataplexy in a group of patients with well characterized NC. Our goal was to investigate the behavioural features, the EMG pattern of cranial and skeletal muscles, and autonomic and EEG variables during cataplexy to shed more light on this puzzling symptom.

2. Methods

2.1. Patients

Seven patients (2 women) suffering from excessive daytime sleepiness and unequivocal cataplexy were included. All fulfilled the diagnostic criteria for NC (American Academy of Sleep Medicine, 2005) and gave informed consent. Non-structured clinical interviews and a preliminary polysomnography (PSG) using the MESAM IV® system (Peter and Penzel, 1994) were used to exclude sleep-related breathing disorders and significant oxygen desaturations. This was followed by a 48 h PSG using a VITAPORT® system [including EEG (C3-A2, C4-A1, O2-A1), right and left electro-oculogram, chin superficial EMG, right and left tibialis anterior EMG, ECG], followed by a multiple sleep latency test (5 nap MSLT) to objectively confirm the diagnosis of narcolepsy. A short sleep latency and at least two sleep onset REM periods (SOREMPs) at MSLT were present in each patient. HLA-DQB1*0602 phenotype was positive in five patients, and CSF examination showed low/undetectable levels of hypocretin-1 in 6 patients and intermediate level in one patient. At the time of this study, none of the patients was taking any medication: three patients were drug naive, and four had suspended drugs for at least two weeks. Mean age was 24.9 ± 17.8 years (range: 12–63). Mean Epworth Sleepiness Scale (ESS) (Johns, 1991) was 16 ± 3 (range: 12–20; n.v. $\leqslant$ 10)] (Table 1). Though patient 6 was HLA-DQB1*0602 negative, his CSF hypocretin-1 level was the highest and his ESS score the lowest in the group (Table 1), he had no other sleep disorder, medical or neurological disorder, mental disorder, medication use or substance use disorder to explain the clinical picture, and according to the International Classification of sleep Disorders (American Academy of sleep Medicine, 2005) he was diagnosed as suffering from NC.

2.2. Neurophysiological investigation of the cataplectic attacks

All patients underwent daytime standardized videopolygraphy (VPG) using a video synchronized with a 21-channel Grass polygraph [including EEG, right and left electro-oculogram, EMG activity from chin and different facial, neck, trunk and upper and lower limb muscles (i.e. mylohyoideus, masseter, sternocleidomastoideus, posterior neck, deltoideus, biceps brachialis, rectus abdominis, thoraco-lumbar paraspinalis, rectus femoris, biceps femoris, tibialis anterior, gastrocnemious), ECG, and thoraco-abdominal respirogram] connected to a computerized system (Neuroscan®, Herndon USA) for off-line analysis of acquired data (16 bit resolution, sampling rate 1024 Hz; EEG band-pass 0.1–60 Hz; EMG band-pass 50–300 Hz). Blood pressure (BP) was monitored using the FINAPRES® (FINger Arterial PRESsure) system, allowing continuous indirect, non-invasive measurements of beat-by-beat blood pressure (Wesseling et al., 1986), and oxygen saturation through finger pulse oxymetry. To assess electrodermal activity, i.e. the changes in skin resistance to electrical conduction induced by sympathetic cholinergic sudomotor function which are considered a sensitive index of bodily arousal related to emotion and attention, spontaneous sympathetic skin response (SSR) was recorded with surface electrodes applied on the dorsal and ventral aspects of the left hand (Liguori et al., 2000; Vetrugno et al., 2003).

The laboratory was also equipped with a microswitch-fitted tendon hammer, an auditory ambient stimulator, wrestling mattresses and a comfortable armchair. A television set showing humorous movies selected according to previously obtained patient preference was used to trigger the cataplectic attacks. Jokes told by patients or examiners were also used as triggers. Patients were standing with at least one examiner close by to prevent any possible harm. During cataplexy, tendon jerks and auditory responses (elicited by means of ambient 50 ms tone bursts with a rise-decay time of 5 ms presented at 90 dB) were tested.

Triggering of cataplectic attacks (triggering period) began after at least five minutes of baseline recording (baseline period)

2.3. Heart rate and spectral EEG analysis during the cataplectic attacks.

For heart rate (HR) analysis, the R–R interval was calculated and expressed in seconds, then converted to instantaneous beats per minute (Task force, 1996). To measure EEG spectral bands during cataplexy, Fast Fourier Transform was performed on C3-A2 or C4-A1 leads for 2-s non-overlapping windows. The power spectrum for the following EEG frequency bands was obtained for each time window: delta = 0.5–4.0 Hz; theta = 4.5–7.5 Hz; alpha = 8–11 Hz; beta = 15.5–29.5 Hz; gamma = 30–60 Hz; and sigma spindle frequency = 11.5–15 Hz.

3. Results

Eighty-five cataplectic attacks were recorded overall in the seven subjects, all of them classified on the basis of their behavioural aspects. Forty-four episodes (52%) resulted in a complete collapse of the patient to the ground; the remaining 41 were more restricted and classified as segmental (i.e. without body fall). Twenty of the 44 cataplectic attacks that ended with a complete collapse of the patient to the ground were preceded by segmental cataplectic attacks (see below).

3.1. Behavioural features of the cataplectic attacks

Cataplectic attacks were triggered by watching an humorous movie or listening a joke, and often occurred in anticipation of the punch line. Cataplexy involved either selected muscles or the entire voluntary musculature. Visually, the jaw sagged, facial muscles suddenly became weak, eyelids dropped (Bell's phenomena was evident in some patients), head fell forward, speech slurred, arms dropped to the sides and knees buckled when cataplectic attacks involved cranial, upper or lower limb muscles. Cataplectic attacks with involvement of the entire voluntary musculature resulted in a body fall to the ground. Therefore, the severity and extent of cataplexy could range from a state of absolute powerlessness with involvement of the entire body (i.e. *global cataplectic attacks*), to a segmental fleeting weakness (i.e. *segmental cataplectic attacks*). The attacks could even be so subtle as to pass unnoticed by nearby observers, but reported by patients as an "inner" feeling. All patients displayed both segmental and global cataplectic attacks. Moreover, some segmental attacks associated with *joint flapping-down motion* could flow into a global attack with body collapse (mixed attacks). As a result, three types of cataplectic attacks were identified, segmental, global and mixed, and could occur in the same patient.