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# Video-EEG analysis of ictal repetitive grasping in "frontal-hyperkinetic" seizures

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**ABSTRACT –** The aim of this study was to obtain a qualitative and quantitative description of the phenomenon of forced prehension during epileptic seizures (ictal grasping- IG) with hyperkinetic semiology. We analysed retrospectively the presurgical, video-EEG recordings of 35 "frontal hyperkinetic" seizures (FHS) in 14 patients (age range: 9-48 years) evaluating the features of ictal grasping by means of off-line, frame-by-frame video-analysis. Ictal grasping was observed in 97.1% of the frontal hyperkinetic seizures in 100% of the patients, with a mean latency of 3.2 seconds with respect to seizure-onset; a mean number of 7.7 IG per seizure were detected. During the same FHS, both arms could perform IG in an alternating fashion. Grasping was usually preceded by a reaching movement and followed by holding or pulling. The sites of prehension were restricted to relatively few sectors, either on the patient's body (45.5%) or the peri-personal space (54.5%). In some cases, the grasping was elicited by hand touching. We did not find a consistent relationship between side of hand grasping and side of ictal EEG discharge or MRI lesion. In conclusion, ictal grasping is an extremely frequent clinical manifestation during FHS. It was an early, forced and repetitive motor behavior, without a clear lateralizing value. Ictal grasping appeared with consistent semiological features, similar to voluntary prehension, suggesting a probable ictal release of physiological grasping behavior.
*[Published with video sequences]*

**Key words:** grasping, hyperkinetic seizures, ictal behavior, frontal lobe, frontal seizures

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Frontal lobe seizures can be characterized by heterogeneous, ictal motor manifestations. In recent years, an epileptic syndrome, with seizures of frontal lobe origin occurring mainly during sleep, was identified with ictal, frenetic, semi-purposeful, bi-manual and bi-pedal automatisms (Waterman *et al.* 1987, Wada 1989, Jobst *et al.* 2000) and its genetic aspects described (Scheffer *et al.* 1995, Oldani *et al.* 1998, Provini *et al.* 1999). The present study stems from the recent observation that "ictal grasping" (IG), defined as a uni-manual or bi-manual forced object prehension, occurs frequently during frontal lobe, "hyperkinetic" seizures, compared to other seizure types (Gardella *et al.* 2006); the term hyperkinetic is adopted from Blume *et al.* (2001).

The aim of the present work was to investigate the characteristics of IG during FHS. In particular, we tried to

establish whether ictal grasping occurred (1) as a reactive, purposeful, ictal motor manifestation, (2) as a compulsive motor behavior or (3) as an ictal, possibly lateralizing, automatism.

## Materials and methods

We reviewed the video-EEG/polygraphic monitoring of 14 consecutive patients (9 males and 5 females; age range: 9-48 years), with drug-resistant frontal lobe epilepsy and hyperkinetic seizures. We refer to hyperkinetic seizures adopting a terminology that relates the ictal semiology to anatomo-functional structures, not necessarily implying that these structures represent the ictal onset zone (Tassinari *et al.* 2003).
Exclusion criteria were seizures with only subjective sensations and seizures with minimal motor manifestations (*i.e.*, paroxysmal arousals, Montagna 1992); 35 seizures were selected. Neurophysiological data were recorded using a 32-64 channel computerized video-EEG system (Telefactor Corporation, West Conshohocken, Pennsylvania, USA). EEGs were recorded according to the 10-20 International System; overnight polygraphic recordings, applying extra-numeral EEG (sovra-orbital, zygomatic) electrodes were performed in 12 patients. High resolution video images were stored on super-VHS or U-MATIC tapes, with an acquisition rate of 25 frames/minute (40 millisecond inter-frame interval). Frame-by-frame video analysis for detailed characterization of the timing of the ictal manifestations was carried out in all seizures. Handedness was evaluated by the Italian version of the Edinburgh Handedness Inventory (Oldfield 1971) in 12 patients, and by interview with either the patients themselves or their relatives in the remainder. Brain MRI was performed in all patients and two had a CT scan**;** nine patients had lesions in the frontal lobe (dysplasia or non-specific). Three patients underwent cerebral SPECT (2 ictal and interictal, one only interictal). Four patients underwent surgical treatment at the "C. Munari" Epilepsy Surgery Center at Niguarda Hospital in Milan or at the Department of Neurosciences at Bellaria Hospital in Bologna; Postoperatively, three of them were Engel class 1a; in one of these patients, the ictal onset zone included ipsilateral temporo-insular structures.

### Data analysis

We defined ictal grasping as an ictal motor manifestation characterized by a forced prehension of an object or body segment. We investigated: (a) IG prevalence; (b) latency of onset of the first IG after clinical seizure-onset and the duration of each single grasping; (d) IG repetitivity, *i.e.* the total number of grasping movements during the same seizure; (e) IG sites of prehension; (f) side of the grasping hand, and its correlations with patient's handedness and side of EEG focus/MRI findings; (g) IG behavioral aspects, namely reaching and/or pulling movements, preceding and/or following the grasp respectively. We excluded hand movements consisting of closure of the hand to make a fist, especially when associated with stiffening of the whole upper limb, object prehension associated with "rubbing" and gentle manipulation, and, obviously, movements performed to push the button of the seizure alarm system or prehension movements on request of the examiner. We did not make any attempt to correlate IG with concomitant EEG discharges, except for IG lateralization.

## Results

### Ictal grasping prevalence

Ictal grasping was observed in 34 (97.1%) FHS in 14 (100%) patients, *i.e.* IG was observed in all recorded FHS but one, and in all patients.

### Ictal grasping features

*Latency, repetitivity and duration*

The first IG appeared after 3.2 ± 3.8 seconds; frontal hypermotor seizures with ictal onset zone including temporo-insular regions had the longest IG latencies. Ictal grasping tended to occur in a repetitive fashion: indeed, in the seizures with grasping, the mean number of IG per seizure was 7.7 ± 5.4 (the differences in the number of IG per seizure were in part due to differences in seizure duration). The mean duration of each grasping movement was 3.1 ± 6.1 seconds.

*Sites of prehension*

Grasping was directed to a limited number of prehension sites that could be either on the patient's body, *i.e.* self-grasping (45.5%), or on fixed points in the patient's peripersonal space (54.5%) (*figure 1* and video sequences). The most frequent prehension sites were: bedside (21%), back of the head/pillow (17%), thigh (12%), headboard of the bed (7%), buttocks (6%), genitals (4%) and popliteal region (3%). Self-grasping did not appear to be context dependent, but looked like a, quite stereotyped, ictal compulsive behavior. In patients with extremely stereotyped frontal hypermotor seizures, IG with the same hand was directed to the headboard of the bed, whereas in other seizures it was directed to the back of the head. In both cases, the patients were simultaneously performing overt pelvic thrusting and rolling movements; grasping the headboard of the bed prevented them from falling onto the floor, whereas a fall occurred when patients grasped the back of their heads (see video sequences). This confirmed the general impression that IG was performed as an automatic motor sequence more than as an adapted movement for protection. Although often aware, the patient was usually unable to control this ictal behavior. The same

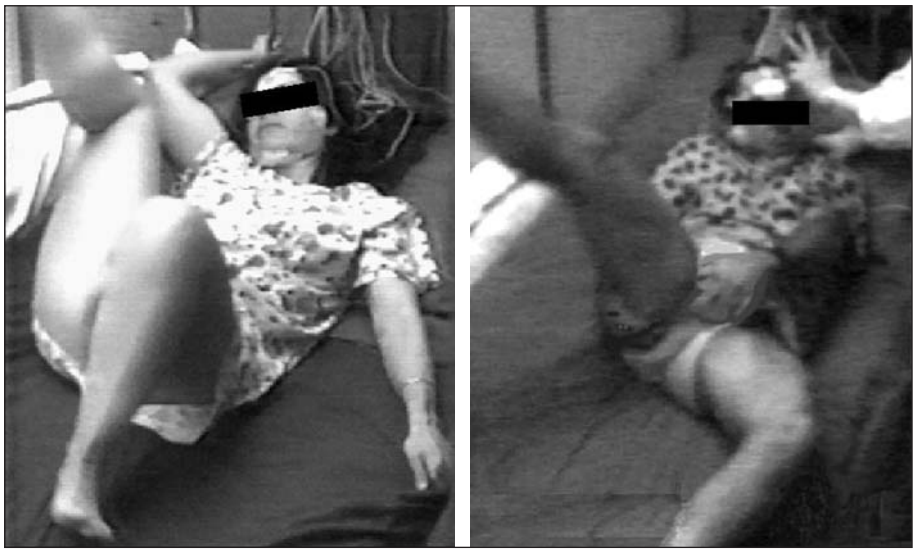

**Figure 1.** Peri-personal and self-Ictal grasping in frontal hyperkinetic seizures.

movements producing the IG, occurred stereotypically as regards timing and features in FHS, in the same patient, recorded in different years *(figure 2)*.

*Lateralization*

We investigated whether one hand preferentially performed IG in each patient, and whether there was a relationship with the patient's handedness, with the side of the EEG focus or the MRI lesion (EEG/MRI side). Considering the total number of IG performed by each patient, no significant side-prevalence was observed. The hand contralateral to the side of the epileptic focus stopped grasping in the late part of the seizure in five patients, being blocked in a dystonic posture, whereas the other hand kept performing IG *(figure 3)*.

We also explored the possible lateralizing value of the first IG (f-IG). The side of the f-IG did not seem to be affected either by patient handedness or by the EEG/MRI side. Indeed, we did not find a significant correlation with any of these parameters in 13 out of 14 FHS patients. In the remaining, eight out of 9 f-IGs were performed with the hand contralateral to the EEG/MRI side.

In general, our impression is that IG is not reliable for the lateralisation of the EEG focus, except for the late phase of the seizure when it could become ipsilateral to seizure focus in association with contralateral dystonic posturing.

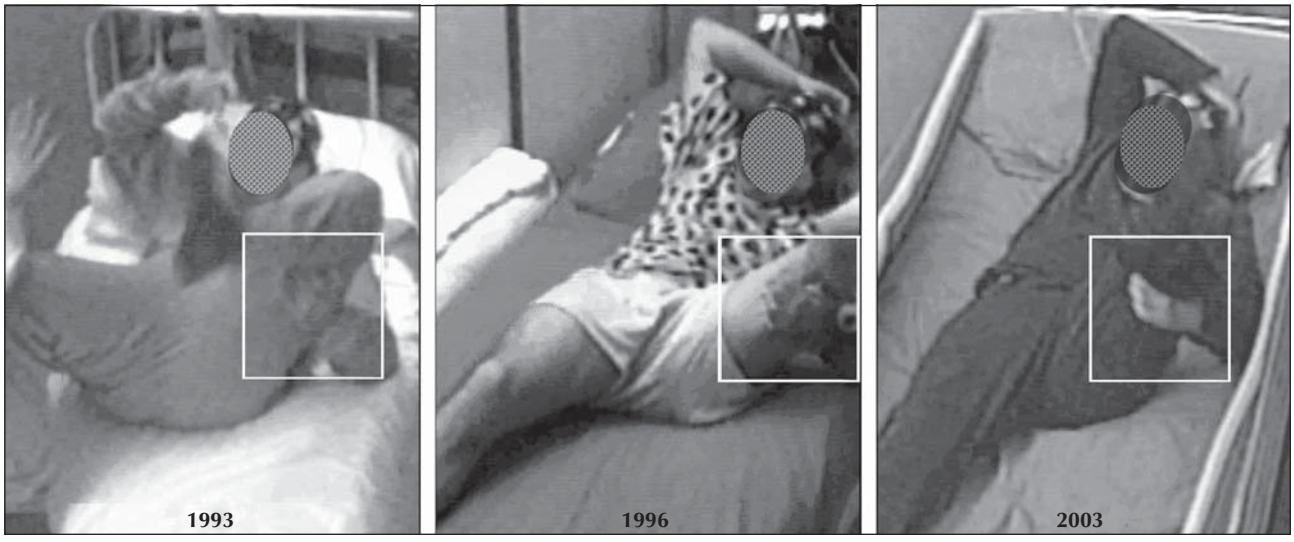


**Figure 2.** Stereotypy of ictal prehension in FHS. IGs in three different seizures of the same patients over a time span of ten years. The frames have exactly the same latency as at the clinical, seizure-onset. The squares in the pictures indicate a clumsy, whole-hand grasping.

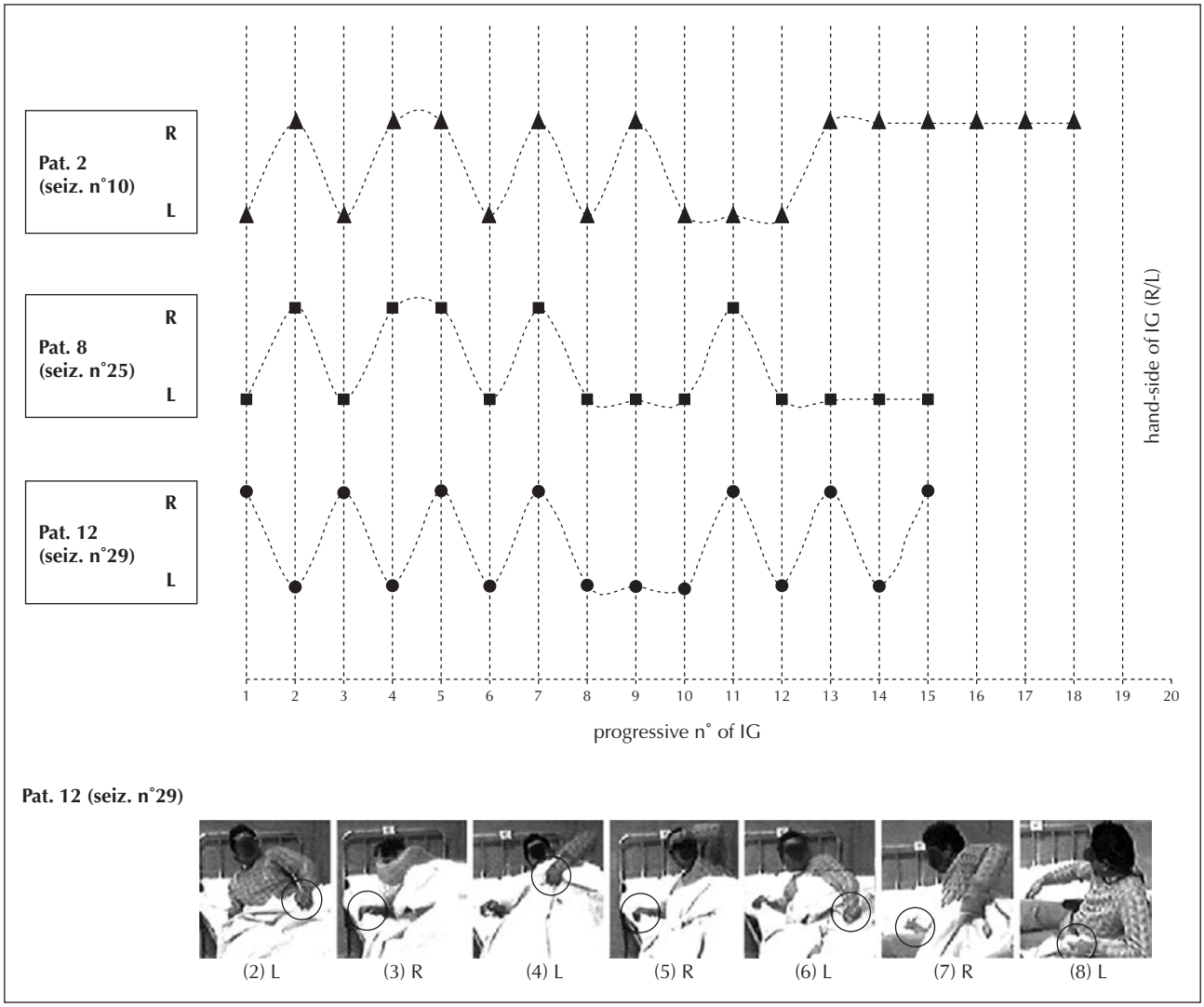


**Figure 3.** Alternating hand side of IG during FHS. The graphs illustrate grasping with right (R) and left (L) hand in three FHS of different patients. The traces indicate only the ordinal sequence of appearance of IGs performed with right or left hand, regardless of their duration and latency. A regular left/right alternating pattern is evident, particularly in the first part of the seizures. In patients 2 and 8, disappearance of grasping in one hand was due to the occurrence of a dystonic posturing in this limb. The pictures document part of the ictal sequence of grasping, relative to the lower graph; IGs are indicated by circles. Grasping with one hand is usually followed by pulling; in some cases, this action continued after the appearance of the following contralateral grasp, as seen in frames 6 and 7 for IG 5 and IG 6 respectively.
R = IG with the right hand; L = IG with the left hand; (n) = progressive n° of IG.

## Behavioral observations

Physiological grasping in primates (Jeannerod 1984, Rizzolatti and Fadiga 1988) consists of three steps: (a) reaching, *i.e.* the arm movement bringing the hand close to the prehension site, (b) grasping, consisting of a progressive opening of the hand, followed by closure to make a fist, and (c) holding/pulling, a prevailing proximal movement of the arm, causing mobilisation of the object grasped. In frontal hypermotor seizures, ictal grasping maintains the characteristics of a complex, highly coordinated, motor behavior, preceded by reaching in 90.5% of cases and accompanied by pulling in 74%. Reaching movements appear to be accurate and are accompanied by a preparatory opening of the fingers, as in physiological grasping movements. Then, a forced, clumsy, whole-hand grasping follows, characterized by finger flexion on the palm of the hand, with inconstant utilization of the thumb (*figure 2* – detail). In 98% of FHS, right and left prehensions started asynchronously on the two sides. A hallmark of IG was the tendency for the movement to be performed by alternate hands (*figure 3* and video sequences). In 2%

of FHS, the first grasping movement was performed with both hands, synchronously and was directed to the same sites with respect to the longitudinal body axis.

## Discussion

Ictal grasping is an early manifestation in FHS, characterized by extremely high prevalence (97% of FHS and 100% of patients), repetitivity and stereotypy in timing and features.

The latency of IG, with respect to clinical seizure onset, was very short in all patients apart from one, whose ictal onset zone extended to the temporo-insular cortex. The latter finding might reflect a possible origin of epileptic activity in temporo-insular areas, subsequently spreading to fronto-parietal structures and thereby allowing the appearance of compulsive grasp. Indeed, recent papers describe hyperkinetic seizures related to discharges arising from the insular or temporal cortices (Ryvlin *et al.* 2006, Nobili *et al.* 2004).

Current knowledge of the physiology of grasping recognizes the roles of separated fronto-parietal circuits, organised in parallel with partial overlap (Jeannerod 1984, Rizzolatti and Fadiga 1988). Intracerebral electrical stimulation of the gyrus cinguli was successful in eliciting a grasping behavior (Bancaud *et al.* 1976). This observation was construed as evidence that the anterior gyrus cinguli plays a major role in processing archaic and highly integrated behaviors with instinctive-affective features. This hypothesis was supported by evidence of "instinctive tactile grasping and placing" in patients with mesial frontal lobe lesions (Seyffarth and Denny-Brown 1948). In addition, IG during FHS was characterized by a high rate of repetition during the same seizure (mean 7.7 events per seizure) and a short duration of each grasp (3.1 seconds).

Ictal grasping has also been observed in other seizure types, but it was either very infrequent (in SMA seizures) or a late and not stereotyped manifestation (in extra-frontal seizures) (Gardella *et al.* 2006). The cyclic repetition of compulsive motor automatism is a semiological characteristic of frontal hyperkinetic seizures (Wieser *et al.* 1992, Riggio and Harner 1995, Lüders *et al.* 1998, Blume *et al.* 2001). Therefore, we can conclude that repetitive IG is a hallmark of frontal lobe seizures with hyperkinetic motor features.

Generally speaking, IG during FHS was not a significantly lateralizing ictal manifestation. The side of the first or most used hand for grasping was neither significantly affected by the side of the epileptogenic area and/or brain lesion nor by handedness. The latter is surprising and could suggest an automatic movement. Indeed, for voluntary reaching/grasping movements, a preferential use of the dominant hand, modulated by context-dependent variables, has been described (Fischman 1998, Gabbard and Rabb 2001). The equivalent use of the dominant and non-dominant hand in FHS supports the hypothesis that frontal IG is an "automatic" movement, as also suggested by its compulsivity and the restricted number of prehension sites. In fact, IG compulsively performed mainly to the patient's body parts was described by the patients themselves as "I witnessed my own movement" or as an urgency to grip, sometimes associated with fear of falling. Neuroimaging studies have consistently demonstrated the involvement of the orbital frontal region and the frontostriatal pathways, including the gyrus cinguli, in the genesis of compulsive behaviors (Baxter *et al.* 1987, Sawle *et al.* 1991).

During FHS, the act of grasping could be a protective behavior performed by patients to fix themselves to a holding point, while other, concomitant, violent, motor automatisms occurred rapidly, impairing the body's stability (*i.e.*, bicycling, pelvic thrusting, etc.). However, with the same timing in different seizures, similar arm movements could result in self-grasping or in extra-corporal grasping, anchoring the patient to a fixed point. This may suggest that, at least in some circumstances, IG (particularly self-grasping) was an automatic motor behavior performed without purpose or even inappropriately, more than a protective act performed by a patient with consciousness completely or partially retained. Self-grasping in FHS was almost as frequent as grasping directed to extracorporal sites. Lesions to the frontomesial areas can cause a compulsive auto-grasping, presumably due to a calloso-frontal disconnection (Ropper 1982, Kumral 2001).

Grasping requires coding of the intrinsic properties of the objects and the transformation of these properties into a pattern of movements resulting in specific grips (Jeannerod 1984). In monkeys (Rizzolatti and Fadiga 1988, Graziano *et al.* 1994), as well as in humans (Goodale and Milner 1992), this process is mediated by fronto-parieto-occipital circuits. The effects of lesions to these circuits can produce misreaching, failure in hand preshaping or deficit in the control of arms and fingers (Chieffi *et al.* 1993, Gallese *et al.* 1994, Brochier *et al.* 1999). During FHS, grasping was performed respecting the physiological sequence of voluntary prehension, being almost consistently preceded by reaching, and followed in more than 70% of cases, by pulling. Furthermore, in IG as well as in physiological voluntary grasping, the fingers began to shape during the reaching movement of the arm, with a progressive opening of the hand until they "matched the object size" (Jeannerod 1984). None of the known signs of disruption of reaching and grasping were observed during IG in our patients. This implies that, during FHS, a functionally intact circuit physiologically regulating the single components of the grasping movement is abnormally activated or disinhibited.

A purposeful, uncontrollable ictal urge to grope and grasp has been described as "ictal alien hand syndrome" elicited by intracerebral electrical stimulation of the cingulate gyrus and parietal cortex (Leiguarda *et al.* 1993, Kremer *et al.* 2001). It has been speculated that the concomitant ictal appearance of motor automatisms and asomatognosia in the same limb requires the simultaneous deregulation of pre- and post-central cortical areas (Boesebeck and Ebner 2004).

Ictal grasping has occasionally been included among the wide spectrum of frontal lobe ictal manifestations (Talairach *et al.* 1973, Geier *et al.* 1976, Williamson *et al.* 1985, Wada 1989, Fusco *et al.* 1990, Wieser *et al.* 1992, Connolly *et al.* 1994, Chauvel *et al.* 1995, Leutmetzer *et al.* 1999), without investigating its possible specificity for certain seizure types. Only recently has it been proposed as a forced, repetitive frontal hypermotor seizures automatism (Gardella *et al.* 2006). We argue that the eupraxic nature of IG in FHS is probably the reason it has been ignored for such a long time, despite its overt prevalence.

Grasping is an inborn motor behavior (Grillner and Wallen 1985), physiologically present in human newborns and reappearing in pathological conditions involving frontal lobe dysfunction (Adie and Critchley 1927, Seyffarth and Denny-Brown 1948). Grasping in non-human primates is an essential reflex for survival, ensuring the animal's grip to the mother (Eibl-Eibesfeldt 1967, Leutmezer *et al.* 1999).

According to Seyffarth and Denny-Brown (1948), in humans "the grasping of the infant betrays the same characteristics we have described for the clinical signs in adults. Its gradual disappearance indicates a process of control which is acquired slowly in the course of development". This "process of control", mediated by a frontoparietal circuitry (Jeannerod 1984, Luppino *et al.* 1999) with the participation of the basal ganglia (Wenger *et al.* 1999), tends to be an inhibitory control-subserving movement regulation. Since Jackson, it has been postulated that complex automatisms might represent the after-effects of ictal discharges producing transitory deficits of the inhibitory or controlling role of cortical structures (Taylor 1931). We suggest that a release mechanism related to seizures, involving prefrontal and frontomesial areas could be responsible for the transient ictal emergence of repetitive grasping and other stereotyped motor patterns, and are most likely expressions of inborn complex motor behaviors (Tassinari *et al.* 2003, 2005). □

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## Legend for video sequences

***Part 1.*** Ictal grasping in FHS shows a tendency to recur several times, roughly with alternate left and right hands.

***Part 2.*** The prehension of some fixed points (in this case the headboard of the bed) might be interpreted as the search for a holding point during the execution of hyperkinetic activity.

***Part 3.*** However, comparing different FHS in the same patient, it was evident that IG did not always serve holding purposes. In fact, the movement producing the IG was extremely stereotyped in both seizures, but in one case the hand was directed to the headboard of the bed (on the left), whereas, in the other seizure, it was directed to the back of the head (on the right) and the patient fell out of bed.

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