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8:45 AM,
Bankers Heart institute

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Asterixis :

Asterixis as negative myoclonus : beyond "liver flap"– unexpected causes – other ways to elicit – clinical significance – unexpected presentations – unilateral asterixis.

What is Asterixis ?

- Clinical sign described as : an alternative. Arrhythmic movements of flexion and extension of hand at wrist and MP joints due to alternate contracture of flexor and extensor muscles of wrist, when arm is outstretched and wrists are extended.

Really?
MBBS

What is asterixis ?

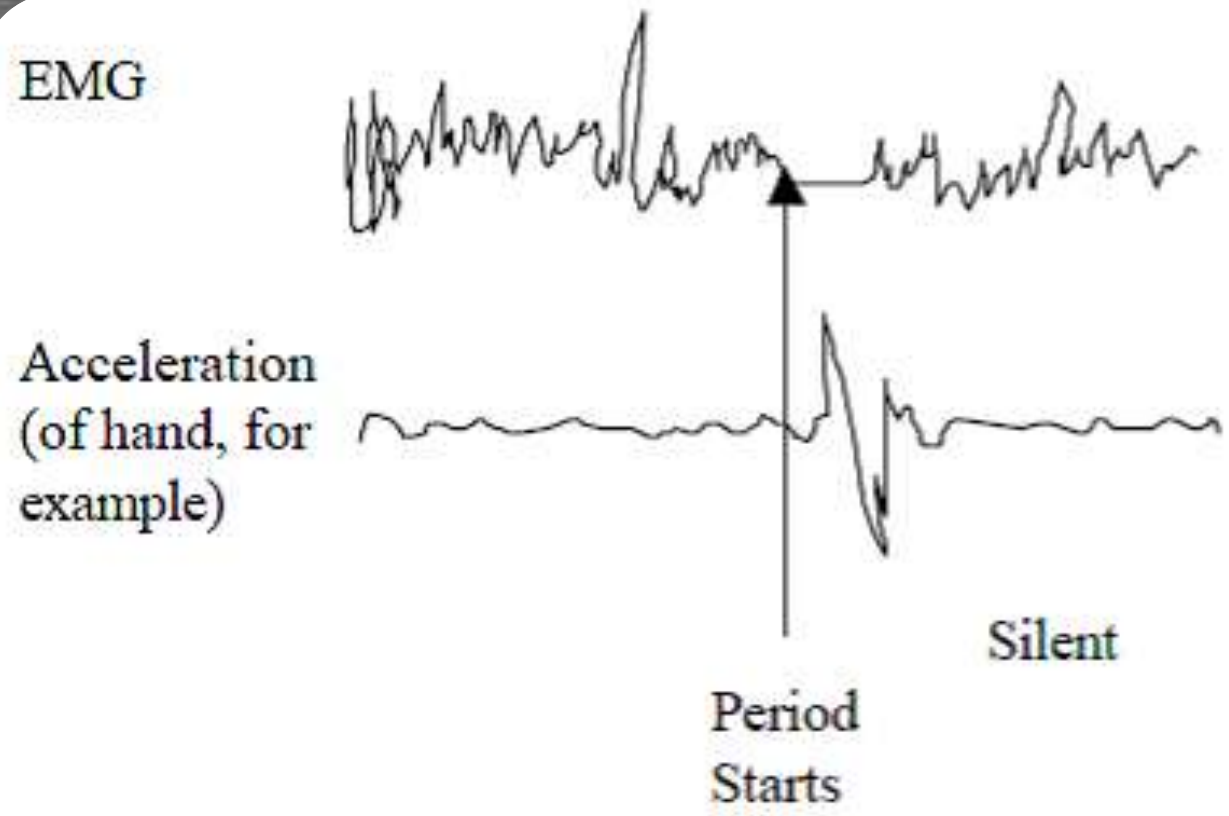
- Asterixis is the inability to sustain posture. It is commonly sought in the upper extremities especially as a diagnostic for impending hepatic encephalopathy. It consists of an intermittent, relatively non rhythmic loss of posture, followed by a regaining of posture.
- 'A'- not able to
- 'Sterixis' - maintain posture./fixed position.

Definition or description?

This definition is from book → Sapira: art and science of clinical disgnosis

What is asterixis ?

- Asterixis is a type of negative myoclonus characterized by irregular lapses of posture of various body parts



An EMG showing normal postural muscle activity suddenly interrupted. At this time, the hands fall, noted by increasing acceleration, until the normal postural muscle activity returns.

Historic background : Asterixis : 1949

- Adams and Foley first described asterixis in 1949 in patients with advanced hepatic encephalopathy.
  - It is a disorder of motor control characterised by brief, arrhythmic interruptions of sustained voluntary muscle contraction usually observed due to brief lapse of posture. It manifests as a bilateral flapping tremor affecting various parts of the body independently and occurs at a rate of 3-5 Hz during active maintenance of posture. **Except for the facial muscles**, the tremors occur in an asymmetric fashion on either side of the body
  - Specialists at Thorndike Laboratory at Boston City Hospital noted abnormal movements in their patients and referred to these as "liver flap." James Foley explained the asynchronous flapping to a Jesuit classics scholar, Father Cardigan while they drank metaxa at the Athens Olympia Cafı. In the conversation, the name "anisosterixis" was coined: An (negative)-iso (equal)-sterixis (solidity). Considering it to be too polysyllabic, Foley and Raymond Adams shortened it to "asterixis." The term came into common parlance, more so because of the influence of Harrison's *Textbook of Medicine*, which had Adams in its editorial board

Historic background : Asterixis :

- Leavitt & Tyler:
- took the next step when they defined the electromyographic (EMG) abnormality associated with what they called metabolic tremor in hepatic encephalopathy.
- As with asterixis, they found brief irregular pauses or reductions in ongoing tonic EMG activity in patients with metabolic tremor.

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Studies in Asterixis

Part I

STEPHEN LEAVITT, MD, AND H. RICHARD TYLER, MD, BOSTON

Although the sudden flap, or lapse of posture, known as "asterixis" has become familiar as a distinct entity, its classic descriptions have always encompassed more than one form of abnormality.

In 1949 Adams and Foley [1] described a "fixed tremor state" in certain patients with liver disease.

Two years later the same authors referred to the phenomena as a "motor disturbance—so unique that it merits a more complete description" (Adams and Foley, 1951).[2] They then suggested that two abnormalities existed, one a "tremor" and the other a "lapse of posture," which they called *asterixis*.

Their description of an electromyographic record suggests a possible interrelationship between the tremor and flap.

Davidson,[4] writing in 1955, used the term "tremor," as Adams and Foley [1] had in 1949, to describe "an arrhythmic, rapid flexion and then restoration . . . ." He described the associated abnormality as an "irregular lateral *movement*" that often appeared before the "tremor itself" (Davidson, 1955).[4] In 1957, Austen [5] called attention to the association of asterixis and pulmonary insufficiency. In this paper a new terminology was suggested, namely, "tremor and twitching"—"the tremor was visible only in the outstretched fingers and had all the characteristics of an action tremor . . ." "coarse twitching movements resulted from the inability to maintain a fixed posture . . . the twitch is identical to that often seen in hepatic coma described under the caption, asterixis" (Austen,[5] 1957). Conn [6] in 1960 incorporated tremor motions and "flapping" into a single phenomenon: ". . . flapping motions give this unique tremor its colloquial name" (Conn,[6] 1960).

Tsukiyama [7] et al, in 1960, did electromyographic studies on ten patients with liver disease and "flapping tremor." They noted the rhythmic discharges noted by Adams and Foley previously and the large variations and irregularity of the discharges. They felt that voluntary or pyramidal factors were important and suggested a cerebral or emotional factor was important in its etiology. They did not distinguish between the tremor and the flap electromyographically.

This paper proposes to describe the patient with asterixis and tremulousness and to discuss certain aspects of these phenomena.

A survey of the frequency of asterixis and related phenomena was made among 125 ward in-patients at the Peter Bent Brigham Hospital. Twelve patients, or 10%, demonstrated asterixis. In addition, all demonstrated a characteristic tremulousness. Three had emphysema, three had cirrhosis, four had uremia, one had a malabsorption syndrome, and one case was unexplained.

Of 24 patients in the recovery room after surgery, asterixis and tremulousness were apparent transiently in five patients.

A subsequent group of five patients were also studied in detail. These had chronic metabolic disorders due to renal or hepatic dysfunction. In this group asterixis and tremulousness presented as nearly isolated phenomena.

Submitted for publication Oct 3, 1963; accepted Dec 4.

Junior Assistant Resident in Medicine, Mary Imogene Bassett Hospital, Cooperstown, NY, Visiting Fellow in Neurology, Peter Bent Brigham Hospital, Boston (Dr. Leavitt); Senior Associate in Medicine, Peter Bent Brigham Hospital, Associate in Neurology, Harvard Medical School, Investigator, Howard Hughes Medical Institute (Dr. Tyler).

This investigation was supported in part by Public Health Research Grant No. FR-05185-01.

Historic background : Asterexis :1995

- Young and Shahani [1995]: were the first to describe unilateral asterixis and they classified the involuntary movements as a form of "mini-asterixis" and the pauses as negative myoclonus.
- Negative myoclonus is characterised by a brief loss of muscle tone in agonist muscles followed by a compensatory jerk of the antagonistic muscles. Asterixis, posthypoxic myoclonus and stiff man syndrome are examples of negative myoclonus. This negative myoclonus correlated with intermittent pauses of 50-200 milliseconds on EMG tracings

Pathophysiology : Multifactorial

- The postural stability or tonic control of the extremities is related to multiple brainstem-spinal pathways such as the vestibulospinal, reticulospinal, or rubrospinal tracts.
- These systems are, in turn, regulated by supratentorial structures.
- The ventro-lateral nucleus of the thalamus is the area in which cerebello-rubral or vestibulocerebellar fibres converge, and is also heavily connected with the prefrontal area.
- There is evidence that the projections from the medial frontal cortex to the brainstem reticular formation may have a role in regulating muscle tone or posture.
- The occasional occurrence of bilateral asterixis and the transient nature of the symptoms suggest that the system regulating posture maintenance is not strictly unilateral. The occurrence of ipsilateral asterixis in patients with cerebellar lesions can be explained by crossing of the cerebello-rubral fibres at the superior cerebellar peduncle.

Despite several postulations, the mechanism of asterixis has not yet been systematically explained.

Pathophysiology :
Metabolism → Toxins →abnormal Neural transmission

The exact mechanism underlying asterixis remains elusive and many explanations have been forthcoming. The following pathogenic mechanisms have been suggested:

1) Result of diffuse, widespread derangement of CNS function.

2) A "receptive inattentiveness to incoming information", which could thus result from a dysfunction of the sensorimotor integration occurring in the contralateral parietal lobe and midbrain.

3) Episodic dysfunction within neural circuits concerned with maintenance of sustained or tonic muscle contraction, due to focal, specific brain lesions or by a generalised neurochemical imbalance. The existence of a possible neural subsystem whose dysfunction could result in asterixis rather than "non-specific" CNS lesions was hypothesised. Drowsiness in normal people and diffuse central nervous system lesions can also produce asterixis, perhaps by their effects on alerting or arousal mechanisms rather than by non-specific CNS actions.

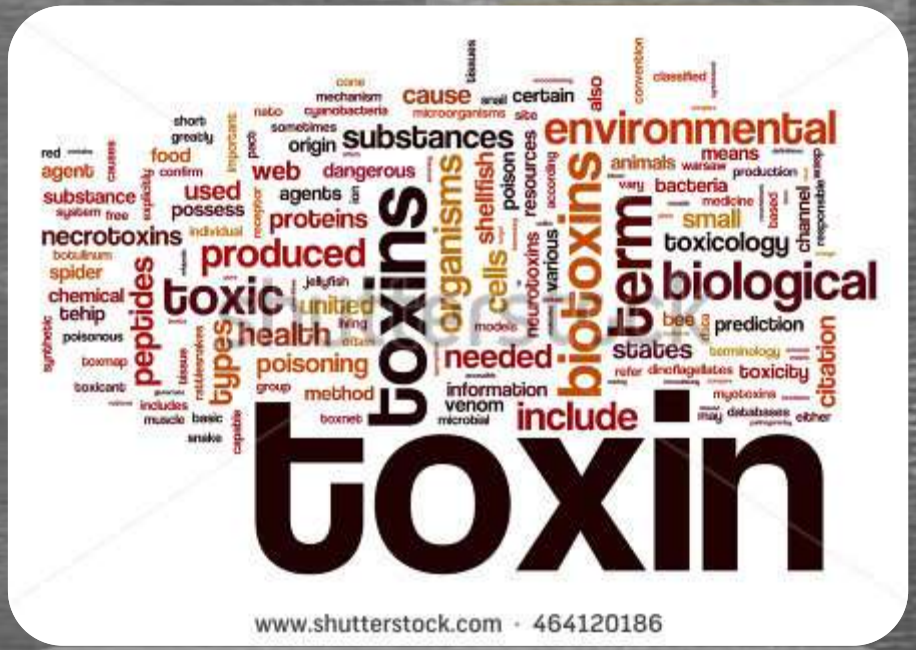
4) Electrophysiological evaluation of asterixis using silent period locked averaging method revealed negative sharp waves in the contralateral central area. It was suggested that asterixis is due to abnormal activity in the motor field in the cerebral cortex

5) Recently mini-asterixis which is a part of the spectrum of the gross flapping tremor seen in hepatic encephalopathy was proposed as being due to the involvement of motor cortex causing a pathologically slowed and synchronised motor cortical wave.

6) A failure in arm posture maintenance that is comparable to failure in leg posture control in patients with astasia. (Astasia means inability to stand due to muscular incoordination).

Which are the systemic toxins?

- Urea
- Ammonia
- Carbon dioxide
- Glucose [hypo-]
- Barbiturates
- Phenytoin
- Others



Interesting → No inflammatory mediators, no infection.

Causes of Asterixis :

- Hepatic encephalopathy
- Co2 Narcosis
- Uraemia : renal failure
- phenytoin, valproate, carbamazepine, metoclopramide, and barbiturates.
- Phenytoin can also unmask latent asterixis due to unilateral lesions and asterixis due to phenytoin has also been referred to as "phenytoin flap."
- Some antipsychotics such as lithium and clozapine and antibiotics such as ceftazidime have been rarely implicated.
- Lithium can cause asterixis at both the therapeutic and toxic plasma levels.

Causes of Asterixis :

Table 1: Causes of asterixis

Bilateral

Metabolic

- Hepatic encephalopathy
- Respiratory failure
- Electrolyte abnormalities
- Heart failure
- Wilson's disease
- Hypoglycemia
- Hypokalemia
- Hypomagnesemia

Drug Induced

- Barbiturates
- Alcohol
- Sodium valproate
- Phenytoin
- Primidone
- Carbamazepine
- Metoclopramide
- Hypoglycemic agents
- Intravenous ammonium chloride
- Gabapentin
- Ifosfamide
- Metrizamide myelography
- Antipsychotics (lithium, clozapine)
- L-DOPA
- Ceftazidime
- Bromide
- Chloral hydrate intoxication

CNS disorders

Vascular

- Intracerebral hemorrhage
- Subarachnoid hemorrhage
- Subdural haematoma
- Cerebral ischaemia

Non Vascular

- CNS infections
- Cerebral lymphoma

Gastrointestinal disease

- Whipple's disease
- Malabsorption syndrome
- Idiopathic steatorrhoea
- Toxic megacolon of ulcerative colitis

Unilateral

- Focal cerebral lesions

Causes of asterixis : unilateral

Bilateral asterixis	Unilateral asterixis
Metabolic: Liver failure, azotemia, respiratory failure	Focal brain lesions at:
Drugs:	Thalamus
Sedatives: Benzodiazepines, barbiturates	Internal capsule
Anticonvulsants: Phenytoin (phenytoin flap), carbamazepine, valproic acid, gabapentin	Corona radiate
Antipsychotics: Lithium	Anterior cerebral artery territory
Antibiotics: Ceftazidime	Primary motor cortex
Others: Metoclopramide	Parietal lobe
Dyselectrolytemia: Hypomagnesemia, hypokalemia	Cerebellum
Bilateral structural brain lesions	Midbrain
	Pons

Asterixis in EXAM : [[not preferred]]

- Questions can be asked on any of the system.
- Pathophysiology difficult to explain
- Patient have it previous day and may not have it on day of exam.
- Method to elicit, always in appropriate: external examiner.

Meaning Of Good Term/ Bad Term?

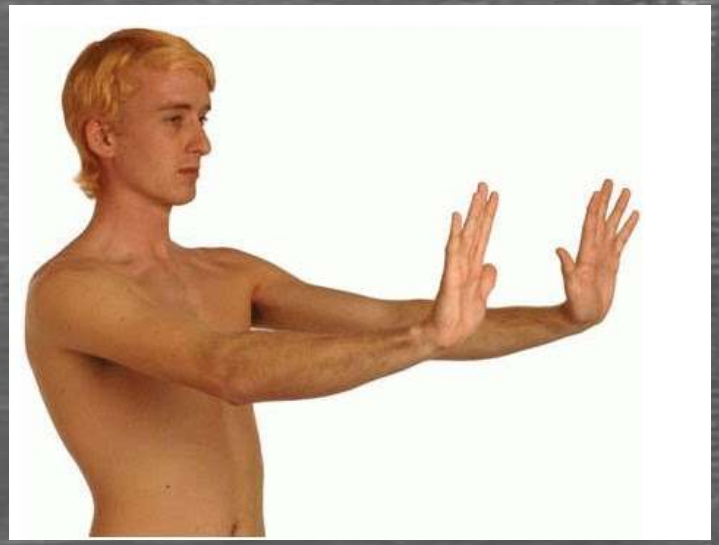
Asterixis in Not "Liver FLAP" : BAD Term

- Asterixis is sometimes referred to as the "liver flap."
- This is a bad term for several reasons.
  - First, there are many aetiologies other than hepatic disease.
  - Second, "flap" implies that the phenomenon occurs only in the hands.
    - Although the hands are most frequently examined for this finding,
- asterixis also may be shown by the fingers, eyelids, tongue, toes, or, for that matter, any part of the voluntary musculature that is required to maintain posture. Finally, the word "flap" implies something rhythmic.

Exception : Facial Muscles : [no antagonists]

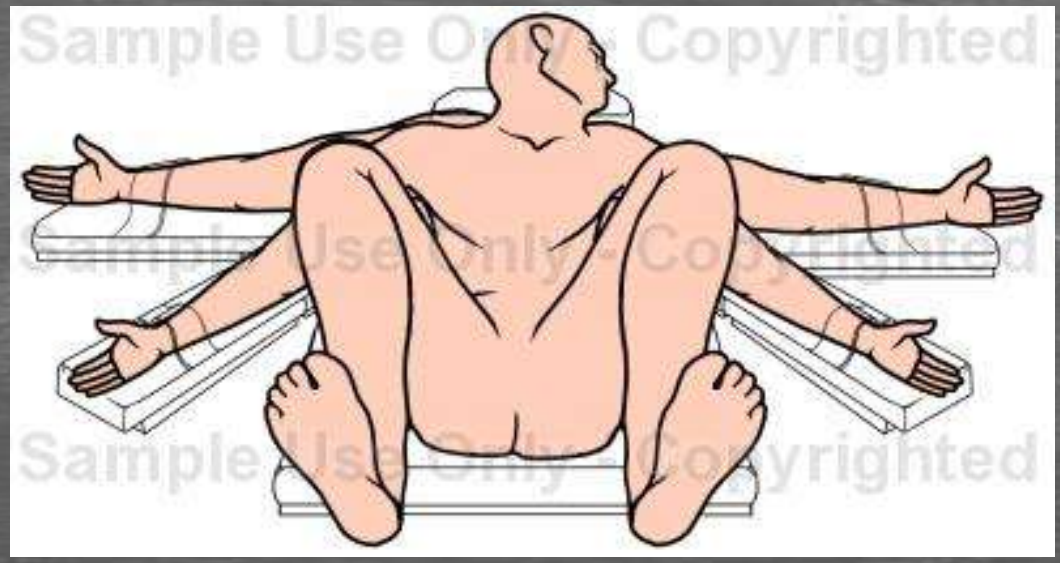
Method to elicit : conventional

- Have the subject extend his raised arms at the elbows and wrists, with the fingers extended and spread. Ask him simply to maintain this posture. Do not consider any rhythmic shaking of the fingers to be asterixis; such movements are tremors.
- Concentrate on lapses in posture, which is quickly regained, then lost again



Methods to Elicit : Lower Limbs

- An alternate method of testing for asterixis involves having the patient relax his legs while he lies supine with his knees bent. The feet should be kept flat on the table and as the legs fall to the sides, watch for flapping of the legs at the hip joint. This repetitively brings the knees back together.



Methods to Elicit : Milkman's Sign

- Dr. Gert Muelheims of Missouri became frustrated with trying to teach encephalopathic patients to keep their hands maximally extended at the wrist for the purpose of demonstrating asterixis, and so he uses a sign described by Dr. Carlos Alberto Leite of Miami. He requests the patient to squeeze the doctor's hand or the doctor's extended fingers. Patients who are unable to maintain a posture are unable to maintain a steady squeeze. The characteristic movements, rapid and arrhythmic, occurring in bursts, can be seen as well as felt (Leite, 1966).

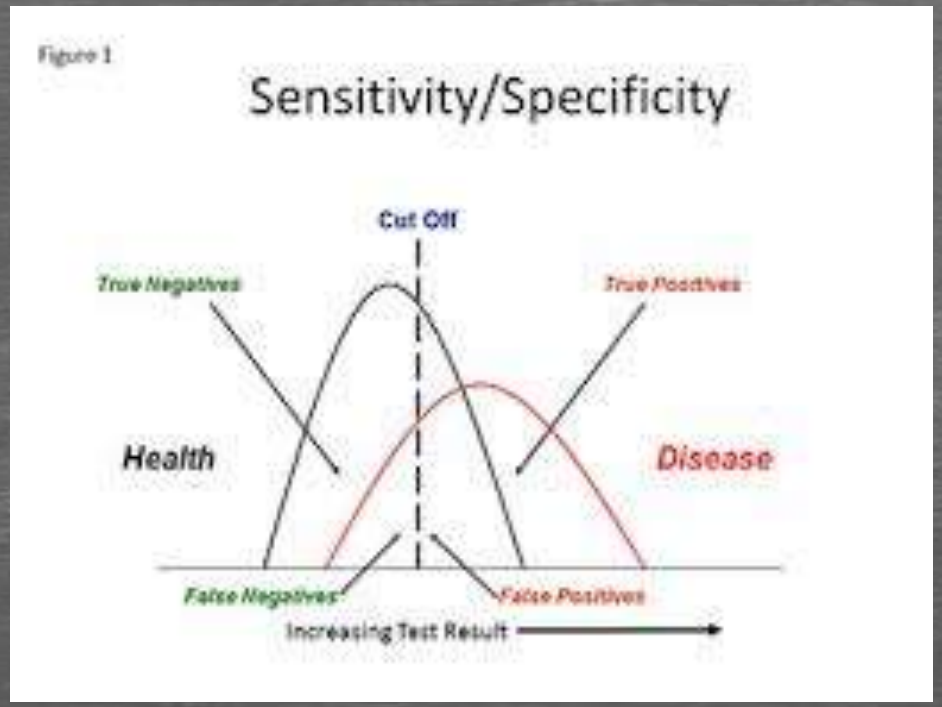
Not to confuse with chorea.

Methods to Elicit : BP Cuff

- Dr. J. Posner of New York has the patient squeeze a semi-inflated blood pressure cuff with instructions to maintain the reading. The readings bounce around dramatically in patients with asterixis.

Significance : specificity & sensitivity

- Asterixis is not specific to any of the disease system
- It is also not sensitive to diagnose any systemic disorder at an early stage. [It may or may not present]



Real Significance: "ADMITTING" Sign : Red Flag

- Although asterixis was discovered in 1949 by Foley and Adams in patients with hepatic encephalopathy, it quickly became obvious that other abnormalities could produce the same lesion. Perhaps the current importance of asterixis is not the length of the differential diagnosis it suggests, but rather its implication that,
- whatever the diagnosis, the condition is at a serious point. For instance, in one study of alcoholic liver disease, asterixis was the only admitting physical finding that had a statistically significant predictive value for mortality, the rate being 56% in those with asterixis, as opposed to 26% in those without it (Hardison and Lee, 1966).

Appearance and dis-Appearance of the sign co-relates with sevearity

Unilateral asterixis : Video

Unilateral Asterixis : causes

- These are most commonly due to focal brain lesions in the genu and anterior portion of the *internal capsule* or ventrolateral *thalamus*. Lesions in the midbrain, parietal cortex, and medial frontal cortex may also cause unilateral asterixis.

Bilateral asterixis	Unilateral asterixis
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Sedatives: Benzodiazepines, barbiturates	Internal capsule
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Dyselectrolytemia: Hypomagnesemia, hypokalemia	Cerebellum
Bilateral structural brain lesions	Midbrain
	Pons

Psudo-Asterixis

- Pseudoasterixis is defined as brief, rapid, voluntary action tremors of the hands and fingers, elicited by slow flexion and extension movements of the hands at the wrists, while keeping the fingers in full hyperextension. Because subtle movements can trigger pseudoasterixis, it mimics asterixis, a primary disorder of muscle tone.

  However in pseudoasterixis, the patient is aware of the hand twitching in contrast to asterixis that is involuntary.

Summary

- Asterixis is an important clinical sign and an invaluable clue to a number of underlying serious diseases.
- It is NOT PATHOGNOMONIC of any condition and therefore a list of possible differential diagnoses tailored to the patient's clinical presentation must be thought of.
- It follows that the treatment of asterixis is the treatment of the underlying condition. However, it should be borne in mind that asterixis is a prognostic marker of severity of underlying disease in some conditions and should therefore be meticulously sought in those cases.
- The early detection of asterixis can help to initiate effective treatment that may help avoid complications in these patients

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Concluded

Asterixis :

Asterexis as negative myoclonus : beyond “liver flap”– unexpected causes – other ways to elicit – clinical significance – unexpected presentations – unilateral asterixis