Jan W. Wijnia, M.D., Ph.D.
Slingedael Korsakoff Centre, Rotterdam

Wernicke-Korsakoff’s: An interdisciplinary view

based on
PhD-thesis: Early detection of mental and motor symptoms in the Wernicke-Korsakoff syndrome

Erasmus MC: Erasmus University Medical Centre
Supervisors Prof. C.L. Mulder
and Prof. A.J.M. Loonen
Co-supervisor A.I. Wierdsma
Content

Background information
- WKS and thiamine deficit
- Theses
- Summary of PhD-thesis

Interdisciplinary view
- Impaired mobility
- Dysarthria
- Acute infections

Neuroanatomical concept of WKS
- Cerebellar neurocognition
- Delirium and cognition

Abbreviation: WKS = Wernicke-Korsakoff syndrome
Jan Wijnia is Elderly care physician employed in Lelie Zorggroep and works at Slingedael Korsakoff centre, Rotterdam

Slingedael is a long-term care facility for people with Korsakoff syndrome

- Manager Korsakoff care in Slingedael: L. Bezemer
- Slingedael participates in Topcare: Prof. A. Postma
- and collaborates with Korsakov Knowledge Center, Rotterdam

- We visited patients in preparation for transferring them to Slingedael Korsakoff centre

- These hospital visits enable us to develop a better understanding of the course of WKS
What happens between chronic alcohol abuse and chronic Korsakoff syndrome is…

… not a gradual event
- WKS is a neuropsychiatric disorder following thiamine deficiency.
- Wernicke encephalopathy is the acute phase of the disease.
- Korsakoff syndrome is the chronic cognitive deficit when the acute phase resolves.
- WKS most often is associated with malnutrition in chronic alcoholism, but may be associated with other conditions that cause nutritional deficiencies.
- The initial phase of WKS is frequently under-reported and under-diagnosed.
- In our patient group, alcohol abuse was on average 31 year long and 5-6 liter of beer per day.
Other causes of thiamine deficiency

- Continuous vomiting
- Food lacking thiamine
- In developing countries: Beriberi
- Bariatric surgery (without vitamin supplements)
- Severe infections, e.g., sepsis
- Hunger strike
- Anorexia nervosa
- Bone marrow transplantation
- Hyperemesis gravidarum
- Other: pancreatitis, leukaemia, palliative care, AIDS-HIV
Consequences of thiamine deficiency

- Vomiting
- Paralysis of nerves that move the eyes
- Polyneuropathy: numbness or tingling (of the feet)
- Vegetative system: low body temperature, rapid heart rate, urinary bladder retention
- Occasionally vision loss (optic neuropathy), hearing loss
- Heart failure

- Bedridden, difficulty **walking**
- **Confusion**, depression, irritability
- Risk of severe **infections**
- Thiamine deficiency can be life-threatening
Gait disorders in alcoholism

Possible causes

- Alcohol intoxication
- Wernicke encephalopathy
- Polyneuropathy (numbness/paraesthesia in feet, vitamin deficiencies)
- Alcoholic myopathy (muscle atrophy, vitamin deficiencies, malnutrition)
- Brain injury
- Stroke (subdural haematoma)
- Cerebellar atrophy (alcohol, thiamine deficiency)
- Brainstem injury (central pontine myelinolysis)
Wernicke encephalopathy
Korsakoff syndrome

Symptoms

1. Memory disturbances (of ‘declaritive’ memory)

2. Behavioural disturbances: disturbances of initiative, planning, organising. i.e., regulating of behaviour (‘executive’, ‘frontal’ brain functions)

3. Impaired awareness of illness (anosognosia)
In practice, Korsakoff syndrome may result in a form of concrete thinking. For instance:

After hospital stay, a patient suffering of Korsakoff syndrome has been staying at the Korsakoff care facility for over two months now.

During an outpatient hospital visit, the patient is told about the results of his gastroscopy, which are normal.

As soon as he gets back to the Korsakoff department, he begins packing his suitcase. With the results being normal, he’s firmly decided to leave and go home.
In the multidisciplinary guideline ‘Disorders in the Use of Alcohol’ (2009), delirium is unfortunately not directly associated with severe thiamine deficiency.

In the DSM-classification of psychiatric disorders ‘Alcohol Withdrawal’ is too easy a label to confused alcoholic patients.

Wernicke encephalopathy is delirium due to thiamine deficiency. Therefore, Wernicke-Korsakoff syndrome is a striking example of delirium associated with subsequent chronic cognitive damage.

The onset of Korsakoff syndrome does not occur gradually.

In patients suspected of having Korsakoff syndrome, a physiotherapist can most effectively determine what is the best time to start a neuropsychological assessment.

A Dutch proverb referring to the ‘back of the head’ expresses a common-sense notion of distinct memory functions exhibited by the ‘hindbrain’.

Fabricated stories (confabulations) in Korsakoff patients show how the brain creates reality if executive functions are being compromised.
Delirium or acute confusional state

Latin: *de* = off, *lira* = tract

Off the tract (derailed)
For instance, delirium in children with high fever
(symptom: unintelligible murmuring)

Symptoms of delirium

- Impaired **attention** with impaired consciousness
- Disturbances of **speech**, language, thoughts
- Symptoms tend to **fluctuate** in severity
Delirium or Wernicke encephalopathy?

1. Difficult to distinguish
   Wernicke encephalopathy is often mistaken for alcohol withdrawal delirium
   Delirium and Wernicke encephalopathy represent parts of the same continuum

2. Concealment of symptoms
   Wernicke encephalopathy is masked by alcohol withdrawal delirium
   Wernicke encephalopathy can mask delirium symptoms

3. Similarity
   Wernicke encephalopathy manifests clinically as delirium
The clinical signs of Wernicke encephalopathy most often occur within hours to days before a subsequent hospital admission. Wernicke encephalopathy may be identified by the presence of a delirium in malnourished alcoholic patients who have trouble walking. In these patients the delirium is usually due to vitamin B₁ deficiency among other causes, which may be erroneously diagnosed as alcohol withdrawal delirium. In Wernicke delirium the possible loss-of-function mechanisms are proposed to come from microglial activation in the brain.

Other heralding symptoms of vitamin B₁ deficiency are the serious infections that are likely to occur. Wernicke-Korsakoff patients who suffered from an infection during the acute phase are at risk of worse neuropsychological outcomes on follow-up. Assessing the final Korsakoff syndrome diagnosis becomes relevant when the patient with suspected Korsakoff syndrome can walk independently again. In an attempt to further understand the overall symptom profile, we proposed a neuropathological correlate for Korsakoff syndrome involving cerebellar neurocognition at brainstem level. The time course of mental symptoms and gait- and balance disturbances is described in more detail.

Muscle weakness in chronic alcoholism may be related to interdependent deficiencies of vitamin D, phosphate, and magnesium. Further research is needed to determine if vitamin D supplementation can improve muscle function in chronic alcoholic myopathy.
How is the time course of the patient’s mobility and mental symptoms in Wernicke-Korsakoff syndrome?
A patient’s mobility and evolving neuropsychiatric symptoms in Wernicke-Korsakoff syndrome (dashed line) with Wernicke-delirium and hospitalisation at 0 months. Assessing the final Korsakoff diagnosis becomes relevant when the patient with suspected Korsakoff syndrome is able to walk independently and unaided (in this particular case at 4 months).

Arrows depict alternative outcomes: further decline, full recovery, or protracted (persistent) delirium.
1. The neurological symptoms of impaired mobility (e.g., ataxia) often go unnoticed in critically ill patients, who are confined to bed.

Patients suffering from delirium of any cause may show impairments of gait during their delirium episode. In the literature little information is available on this particular topic, apart from specifications of psychomotor activity in delirium (Cf., Axer et al, 2010; Godfrey et al, 2009), including

- hyperactive, agitated delirium,
- hypoactive, ‘quiet’ delirium,
- or a mixed, varying form.

2. Dysarthria is another important motor symptom of delirium. Acute delirium may show distinctive dysarthria leading to impairments in intelligibility and audibility of speech (motor speech disorder).

Recognition of the motor symptoms of delirium, including impaired gait and dysarthria, may be helpful to raise the clinician’s index of suspicion about Wernicke-delirium.
DELIRIUM

SYMPTOMS of LANGUAGE and SPEECH

- Slurred speech (and changing intensity of dysarthria)
- Aphasia: Anomia, paraphasia, e.g., ‘bubbling thing’ for urinary drainage bag
- Confusion: incoherence of thoughts / language

Transitions of different linguistic levels and coinciding of motor (dysarthria) and mental (aphasia, confusion) symptoms
Severe infections in the initial stage of WKS

Infections frequently occur in the initial stage of WKS. Most often pneumonia, urinary tract infections. Furthermore, sepsis, abscesses, empyema. Occasionally peritonitis, meningitis.

\[ \downarrow \text{Thiamine} \]
\[ \downarrow \text{Acetylcholine (ACh)} \]
\[ \downarrow \text{Microglial hyperactivity} \]
\[ \downarrow \text{Delirium} \]
\[ \downarrow \text{Cognition} \]
\[ \downarrow \text{Korsakoff syndrome} \]

\[ \downarrow: \text{deficiency, low level, or impaired} \]

Cerebellar Stroke patients*

...may show non-motor deficits:

- Symptoms such as disturbances of memory and orientation, analogous with global dementia
- Symptoms that traditionally are interpreted as frontal symptoms: perseveration, impulsivity, disinhibited behaviour, and increased distractibility
- Incoherence of thought
- Symptoms like fatigue, sleeping disorders, depression, or anxiety

* Personal experience of multidisciplinary stroke rehabilitation, unpublished data of three patients summarised in a paper on an hypothesis of Cerebellar neurocognition in Korsakoff’s syndrome (Wijnia & Goossensen, 2010).
Cerebellar cognitive affective syndrome (CCAS)

- Impairment of executive functions, such as planning, set-shifting, verbal fluency, abstract reasoning, and working memory

- Difficulties with spatial cognition, including visuo-spatial organization and memory

- Language symptoms, including agrammatism and dysprosodia

- Personality change with blunting of affect or disinhibited and inappropriate behaviour

WKS delirium-cognition (hypothesis)

Schematic paramedian view through cerebellum, brainstem, and thalamus.

Superior cerebellar peduncle, marked by left red arrow, crosses over to the (opposite) RN and thalamus. Connections to the olivary nucleus are shown by black arrows. The position of the aqueduct, i.e., the narrow channel connecting the third and fourth ventricle, is indicated by a dotted line.

'Circled' area involved in the symptomatology of Wernicke-delirium and Korsakoff syndrome.


