DIFFERENT TYPES OF DELIRIUM: WHAT ARE THE DIFFERENCES? OR HOW DO WE DIFFERENTIATE BETWEEN THEM AND ARE THERE DIFFERENCES IN OUTCOMES?

Joint Annual Meeting of the Swiss Society of Cardiology (SSC) and the Swiss Society of Cardiac and Thoracic Vascular Surgery (SSCS)
June 10-12, 2015, Kongresshaus Zurich
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DISCLOSURE STATEMENT

Competing interests: none to declare
WHY WE SUBTYPE DELIRIUM?

Delirium is a common neuropsychiatric syndrome with considerable different aetiologies and phenomenological heterogeneity.

It is important to subtype delirium:

- As this could produce homogenous clinical manifestations which possible represent different aetiologies and possible different neuropathological mechanisms.
- Different subtypes could have different treatment and outcomes.

However subtypes of delirium with unique and definitely characteristics are not widely accepted.

Here I will attempt to present the most common subtypes of delirium and I will focus on motor (psychomotor) subtyping as this is the most often discussed and the most obvious in the clinical settings.
SUBTYPING ACCORDING TO A CLEAR AETIOLOGY

• Alcohol or substances withdrawn delirium vs delirium due to a medical condition.

This distinction is widely accepted and it has been implemented in the classification systems. (ICD-10, DSM-IV, and DSM-5)

Alcohol (and substance) withdrawal delirium, or delirium tremens, shares common symptoms with delirium

But severe agitation, tremor and physical symptoms like tachycardia, tachypnoea, and hypertension are often present. In addition withdrawal seizures.

This form of delirium occurs approximately three to five days after the cessation of alcohol consumption.
According to anatomical brain area

1. Cortical vs Subcortical
2. Anterior vs posterior cortical
3. Right vs left hemisphere

All those subtypes arise mostly of studies with delirium after brain injury. However EEG data, Polysomnmography, Evoked potential, CT and MRI techniques showed no clear evidence that there is an anatomical distinction in delirium. Given that areas of the brain are interconnected an anatomical location of delirium is difficult (if not unlikely) to be determined.
ACCORDING TO OUTCOME

1. Reversible or recovered delirium vs no reversible or persistent delirium

2. An older definition was acute vs chronic delirium

Closely related to the concept of ‘recovery’ are issues of ‘response’ (which typically relates to initial reduction in symptom load), ‘remission’ (which typically refers to a sustained initial period without major symptoms) and ‘resolution’ (which usually refers to complete symptom reduction) Adamis et al 2015.
ACCORDING TO SEVERITY AND NUMBER OF SYMPTOMS

- Sub-syndromal (SSD) vs full syndromal (FSD)

- SSD delirium is described as evidence of delirium features without full diagnostic criteria for delirium diagnosis. Accurate definition remains uncertain as it is unclear about the number, type and severity of symptoms required to warrant a label of SSD.

- This leads to categories vs dimensions in the diagnostic philosophy
ACCORDING TO TIME

- Prodromal delirium - delirium - residual delirium

This subtyping also interferes with the classification of subsyndromal vs full syndromal and the recovery process when we are not sure about the onset time.
ACCORDING TO CO-MORBIDITY

Delirium vs delirium superimposed in dementia

Difficult to diagnose dementia in the course of delirium.

IQCODE (information from relatives)
ACCORDING TO PHENOMENOLOGY

1. Psychotic vs non-psychotic

2. Psychomotor/ motor subtypes
PSYCHOMOTOR/MOTOR/VIGILANCE SUBTYPES OF DELIRIUM

Two subtypes recognised since Hippocrates

Phrenitis (hyperactive)

Lethargus (hypoactive)

Hippocrates used the term phrenitis to describe an acute onset of behavioural problems, sleep disturbances and cognitive deficits which were usually associated with fever, while he used the term lethargus to describe inertia and dulling of the senses. He believed that lethargus can change to phrenitis and vice versa. (mixed subtype) Adamis et al 2007
This distinction remained until recently (Lipowski 1989, Camus et al 2000(factor analysis)). Consciousness level was the predominant distinction.

**Three subtypes**

Hypoactive, hyperactive and mixed

Koponen et al 1989; Liptzin and Levkoff, 1992; Meagher et al 1989

A third “mixed” category was added in recognition that many patients experience elements of both within short time frames.
FOUR SUBTYPES

Hypoactive, Hyperactive, mixed and none

O’Keefe and Lavan, 1999; de Rooij et al., 2006; Meagher, 2009 as well as with the assistance of electronic motion analysis (Godfrey et al., 2008; Van Uitert et al., 2011)

Two studies use Latent Class Analysis (Yang et al., 2009; Meagher et al 2014) which confirm the four motor subtypes.

The status of no subtype patients is also somewhat unclear, with studies suggesting that these patients have less severe, or even questionable delirium (Meagher et al., 2012).

However the last two studies also emphasises that motor disturbances lack absolute specificity for delirium since they are relatively common in hospitalized patients without delirium and some delirious patients have only minimal motor disturbances.
STABILITY ACROSS THE TIME OF MOTOR SUBTYPES (LONGITUDINAL STUDIES)

• Subtypes were stable within delirium episodes

Meagher et al 2012 (palliative care); Albrecht et al 2015 (post-operative hip fracture patients); MAPLE study Amsterdam (post-operative hip fracture patients) Adamis et al 2015 (abstract).

Fann et al. (2005) Hypoactive subtype tended to persist through course of a delirium episode

• Subtypes variable? (Slor et al 2013)

Few studies, but seems that motor subtypes are stable during delirium.
PHENOMENOLOGY AND MOTOR SUBTYPES
DO DIFFERENT MOTOR SUBTYPES HAVE DIFFERENT
PHENOMENOLOGY?

Ross et al (1991): hallucinations and delusions more often in hyperactive

Meagher et al (2000): hyper more severe delirium and more often delusions, mood lability, sleep-awake disturbances and variability of symptoms

Gupta et al. (2005): Hyperactive patients had greater sleep–wake cycle disturbance and mood lability. Hypoactive patients had greater language disturbance

De Rooij et al. (2006): medical elderly (2 subtypes hypo vs no-hypoactive) Affective lability less prominent in hypoactive patients.

Leonard et al 2011(palliative care): mixed subtype more severe delirium, more often sleep-awake disturbances, hallucinations, delusions, languages abnormalities

Meagher et al 2011 (palliative care, longitudinal): mixed type more severe delirium: subtypes different only in delusions and affective lability. Mixed subtype more often delusions.
CONTINUE …


Boettger et al 2011: (2 subtypes) hyperactive more severe delirium (MDAS) more impaired cognition, thinking disorganisation, and perception.


Mushtag et al 2015 (2 subtypes) hypoactive delirium more cognitive impairment compared to hyper.
AETIOLOGY (RISK FACTORS) AND MOTOR SUBTYPES

O’Keeffe and Lavan (1999) elderly medical: No difference in aetiological factors

Morita et al (2001), palliative care: hyperactive symptoms associated with drug induced delirium, dehydration relate pathology with hypoactive

Peterson et al (2006) ICU: Hypoactive is associated with older age


Meagher et al (2012) palliative care: hyperactive: younger age, less exposure to corticoids more likely the cause of delirium to be a metabolic disorder.

Franco et al (2014). Disorientation in place and time and visual-construction disturbances predict hypoactive or mixed subtype.
MOTOR SUBTYPES AND TREATMENT

Platt et al. (1994): Response to antipsychotic treatment similar in hypo and hyperactive patients

Hyperalert delirium less amount of haloperidol


MOTOR SUBTYPES AND TREATMENT

Lam et al. (2003) Medication use less in hypoactive subtype

Liu et al. (2004) No differences in response rates between motor subtypes and risperidone treatment

Atalan et al. (2013) In hyperactive delirium after cardiac surgery morphine is superior to haloperidol

Boettger et al. (2014) Response to antipsychotics is similar between hypo and hyper subtypes. Higher dose of antipsychotics needed to control symptoms in hyperactive delirium
MOTOR SUBTYPES AND OUTCOMES

**hypoactive poor outcomes (mainly mortality and function)**


Stransky et al (2011) hypoactive prolonged ICU staying, prolonged mechanical ventilation time

Mohamed et al (2015) hypoactive more cognitive decline and higher mortality

Kobayashi et al (1992), Liu et al (1997): **mixed has the worst outcome**

Marcantonio et al 2002: **Hypoactive better outcomes**
MOTOR SUBTYPES AND OUTCOMES

No difference between outcomes and motor subtypes reported by:

Santana Santos et al 2005; Slor et al 2013; Boettger et al 2014

No conclusive results. It seems that hypoactivity is associated with a relatively poorer prognosis
SCALES / INSTRUMENTS FOR MOTOR SUBTYPING

Actiwatch, Actigraphs studies no conclusive results. Some no relation with subtypes, eg Eeles 2009 others partial (Godfrey et al 2009) and others identify four factors Honma et al (1998)

- Visual analog scales (eg Ross et al. 1991)
- Clinical eg Olofsson et al. (1996)
SCALES / INSTRUMENTS FOR MOTOR SUBTYPING

• DSI Liptzin and Levkoff, 1992

• DAS O’Keeffe & Lavan (1999)

• MDAS eg Marcantonio et al. (2002)

• DRS-R98 e.g. Gupta et al. (2005) De Rooij et al. (2006)

• RASS eg Peterson et al. (2006) Robinson et al (2011)
### DMSS 30 ITEMS, 13 ITEMS AND 4 ITEMS (Meagher et al 2014)

<table>
<thead>
<tr>
<th>Hyperactivity Items</th>
<th>Hypoactivity Items</th>
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<tbody>
<tr>
<td>(1) Increased activity levels</td>
<td>(1) Decreased amount activity</td>
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<tr>
<td>(2) Increased speed of actions</td>
<td>(2) Decreased speed of actions</td>
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<td>(3) Involuntary movements</td>
<td>(3) Apathy / listlessness</td>
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<td><strong>4) Loss of control of activity</strong></td>
<td>(4) Decreased amount of speech</td>
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<td>(5) Restlessness</td>
<td>(5) Decreased speed of speech</td>
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<td>(6) Wandering</td>
<td>(6) Decreased Volume of speech</td>
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<td>(7) Increased speed of speech</td>
<td>(7) Decreased alertness</td>
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<td>(8) Increased amount of speech</td>
<td>(8) Withdrawal/unawareness</td>
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<td>(9) Loud speech</td>
<td>(9) Hypersomnolence</td>
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<td>(10) Abnormal content of verbal output</td>
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<td>(11) Hyperalertness</td>
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<td>(12) Distractibility</td>
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<td>(13) Fear</td>
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<td>(14) Irritability</td>
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<td>(15) Euphoria</td>
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<td>(16) Uncooperativeness</td>
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<td>(17) Combativeness</td>
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<td>(18) Nightmares</td>
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<td>(19) Hallucinations</td>
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<td>(20) Persistent thoughts</td>
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<td>(21) Tangentially / irrelevant talk</td>
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WHY DIFFERENT RESULTS?

1. Different studied populations (ICU, elderly medical, post-operative, palliative care, Liaison referrals) possible biases: Liaison population s more often hyperactive cases, palliative care more often hypoactive, ICU more often mixed subtypes. Non subtype often reported in SSD (Leonard et al 2014).

2. Different categories of motor subtypes have been used e.g.
   
   Hypo vs hyper
   
   Hypo vs hyper vs mixed  
   Power of the study
   
   Hypo vs hyper vs mixed vs none
WHY DIFFERENT RESULTS?

3. Different definitions of motor subtypes

Not purely motor, often psychomotor (behaviour), mixed with levels of consciousness, or alertness or other phenomenology (attention) e.g. abnormal hand movements (carfology, floccillations) or dysgraphia (pure motor phenomena) have been reported in hypo and hyper subtypes (Holt et al 2015)

4. Different methods-instruments for motor subtyping

E.g. clinical, visual analog scales, or items of different scales DSI, DRS, DRS-98R, MDAS, DMSS, DMSS-4. Low agreement between those methods 34% in palliative care (Meagher et al 2008)
WHY DIFFERENT RESULTS?

5. Use of the same scale to assess delirium, delirium severity and motor subtypes

Eg mixed subtypes seems with more severe delirium
IS WORTH TO CONTINUE RESEARCH IN MOTOR SUBTYPES?

Yes!!!!

a) Everyday clinical practise shows that there are different motor subtypes in delirium. If motor scales cannot capture motor subtypes, improvement of the scales is necessary!!!

b) However motor subtypes are not unique to delirium. Motor disturbance not always are due to delirium. E.g. depression, schizophrenia catatonia, manic states.

c) Motor subtyping help in better identification of delirium (hypoactive more often is missed)

d) Perhaps different physiopathology reflected from the different subtypes (domaminergic system involve more with hyperactive, achetylcholinergic more with hypoactive. Pro inflammatory cytokines with sickness behaviour (hypoactivity)
TAKE HOME POINTS

• Not universal agreement how to subtype delirium

• Motor subtyping more obvious

• 4 motor subtypes

• Motor subtypes fairly stable during delirium

• Possible different aetiological factors but not clear link

• Hypoactive perhaps worst prognosis, but often missed
REFERENCES


