Postoperative Confusion and other Cognitive Disorders

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Chair, International Alzheimer’s Association, Anesthesiology Professional Interest Area
Cognitive Disorders

**Community**
- Confusion
- Preclinical Dementia
- Mild Cognitive Impairment (MCI)
- Early dementia
- Dementia

**Perioperative**
- Confusion
- Delirium
- POCD
- Dementia
BRITISH MEDICAL ASSOCIATION.
FIFTY-FIFTH ANNUAL MEETING.

PROCEEDINGS OF SECTIONS.
INSANITY FOLLOWING THE USE OF ANÆSTHETICS IN OPERATIONS.

Read in the Section of Psychology at the Annual Meeting of the British Medical Association held in Dublin, August, 1887.

BY GEORGE H. SAVAGE, M.D.LOND., F.R.C.P.,
Medical Superintendent and Resident Physician, Bethlem Royal Hospital;
Lecturer on Mental Diseases, Guy’s Hospital.

In treating this subject it will be first necessary to clear away, as much as possible, any fallacies which might induce us to attribute too much importance to any one cause in the production of mental disorder. All writers and observers have noticed that it is very rarely that one cause alone is efficient for the production of any attack of insanity, and that usually there are several predisposing causes which may have been in operation for a long time, as well as one or more exciting causes which may have been in action for much shorter periods.

In the subjoined paper I only point out that I have met with a series of cases of insanity in which the use of anaesthetics, in predisposed subjects, has been followed by insanity. To make the matter more clear I have collected together similar cases which have followed similar causes, such as alcohol, belladonna, etc. I think by this means to be able to show that the relationship is truly causal.

I will at once place before you several propositions which I hope to prove.

Any cause which will give rise to delirium may set up a more chronic form of mental disorder quite apart from any febrile disturbance. (a) The most common form of mental disorder which comes on in such cases is of the type of acute delirious mania; (b) though such mental disorder is generally of a temporary character, it may pass into

that delirium accompanying symptoms. After scarlet fever or such disorders. Thus, one young active, two of whose sisters were covered, and whose mother, too, to periods of extreme mental perturbation. After fever, early in the disease because of excited sleepless delirium, her chatter assumed a more organized but with less incoherency; ere long it was difficult to prevent her from doing and condition rapidly passed. When she was removed to Bethlem, with violence and weakness, she passed through exhaustion—stupor—from which she has remained well ever since. At the same age, two of whose sisters, with a very eccentric father, had died of measles, of which she died in.

After the delirium of pneumonia, conditions may start an insanity. In those who come of insane stock, and having contracted, and that having contracted, they are likely to have early and severe attacks.

Besides alcohol and fever, belladonna proved efficient in a girl belonging to a very nervous family. Belladonna liniment instead of a medical man treated her delirium, but at the end of that time she was called in to see her. The mania of the delirious type; extreme. As in most of the cases at the end the girl recovered. For saying that any toxic agent, no matter what, can produce the delirium of the nervous system, belladonna, will cause temporary insanity, especially in the nervously unstable.
Back to the future...

Any cause which will give rise to delirium may set up a more chronic form of mental disorder quite apart from any febrile disturbance. (a) The most common form of mental disorder which comes on in such cases is of the type of acute delirious mania; (b) though such mental disorder is generally of a temporary character, it may pass into chronic weak-mindedness, or it may pass into (c) progressive dementia which cannot be distinguished from general paralysis of the insane.

To return to the first group, then; any cause producing delirium...
Outline

- Demographics
- Confusion and Delirium
- Are they preventable?
- Risk Factors including Dementia
- How does this fit with POCD?
In Australia (2010)

- 13% population are 65y or older
- 1.1% population have dementia
- Elderly people often need surgery and anaesthesia

but if you are 65y or older.....

- One third of anaesthetics
- Delirium incidence up to 65%
- Cognitive decline incidence up to 42%
- Nearly 10% have dementia
Proportion of population over 65 and anaesthetics administered

<table>
<thead>
<tr>
<th>Year</th>
<th>% population 65y or more</th>
<th>% anaesthetics 65y or more</th>
</tr>
</thead>
<tbody>
<tr>
<td>2001</td>
<td>12.4</td>
<td>25.1</td>
</tr>
<tr>
<td>2002</td>
<td>12.7</td>
<td>25</td>
</tr>
<tr>
<td>2003</td>
<td>12.8</td>
<td>28.5</td>
</tr>
<tr>
<td>2010</td>
<td>13.5</td>
<td>32.2</td>
</tr>
<tr>
<td>2051</td>
<td>24.2</td>
<td>48.4</td>
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</table>
Confusion and Delirium

- **Confusion:**
  - Loss of orientation
  - Often with loss of memory

- **Delirium:**
  - State of confusion
  - Altered consciousness
Confusion Definition

- Loss of orientation
  - Where
  - When
  - Who
  - What

- Often with loss of memory
Confusion and Agitation in PACU
“Emergence Delirium”

Risk Increased: Baseline deficit, Benzodiazepine premed, Breast Surgery, Abdominal Surgery, Long Case

Lepousé C, Lautner CA, Liu L, Gomis P, Leon A.
Management of Confusion in PACU

Look for the cause!

• Assessing Consciousness
  – Residual Sedative Drug Effects
    (Flumazenil / Naloxone / Time)

• Pain control

• Other irritants
  – Bladder
  – Pressure

• Antipsychotics
  – Haloperidol
A calm, tranquil environment...
Delirium - When

- Different to ‘emergence delirium’

- Usually occurs after:
  - Smooth emergence
  - Lucid period
  - Postoperative days 1-3
Delirium Definition

- Two subtypes:
  - Hyperactive (agitation)
    - More easily recognised
    - ~ 25% of cases
  - Hypoactive (lethargy)
    - Less recognised but more common
    - Up to 70% of cases following hip fracture repair
    - Higher mortality
Delirium - What

Confusion and altered consciousness...

– Acute/rapid onset
– Fluctuating Course
– Overlap with Cognitive Problems
– Often identifiable cause
– Clinical Significance
– Lack of Baseline Assessment

Detection of cognitive recovery from delirium assumes stable cognitive baseline
Delirium – Why (Predictors)

Noncardiac Surgery

• Age
• Cognitive impairment
• Physical function
• Abnormal biochemistry
• Alcohol abuse
• Thoracic surgery
• Aortic aneurysm surgery

Cardiac Surgery

• Cognitive impairment
• Hypoalbuminaemia
• Depression
• Prior stroke or TIA

A previous episode of delirium

Rudolph 2011
Measuring Delirium

- Psychiatric assessment
- Confusion Assessment Method (CAM)
- Delirium Symptom Interview
- Delirium Rating Scale (DRS)
- Memorial Delirium Assessment Scale (MDAS)
- Confusion Assessment Method for ICU (CAM-ICU)
Identifying Delirium

Confusion Assessment Method (CAM)

Feature 1: Acute Onset & Fluctuating Course

Assessment
- Preoperative baseline cognitive function
- Postoperative daily or more frequent cognitive assessment

Feature 2: Inattention

Assessment:
- Days of the week / Months of the year backward
- Digit Span
- Serial 7’s

Feature 3: Disorganized Thinking

Assessment:
- Illusions, Delusions, possibly hallucinations
- Question patient about illogical ideas (see CAM-ICU)

Feature 4: Altered Level of Consciousness

Assessment:
- Richmond Agitation and Sedation Scale (RASS)
- Monitor level of consciousness

DELIRIUM

Rudolph 2011
Incidence of Postoperative Delirium

- All patients: 10 – 30%
- Elective orthopaedic: 9 – 15%
- PFF: 35 – 65%
- Cardiac Surgery: 37 – 52%
- Elderly patients: 30 – 60%

34% - 68% unrecognised

Rudolph 2011
Delirium - Impact

• Increased length of stay
• Increased costs
• Increased mortality
• Stressful – family and patient
• Reduced functional recovery
• Risk factor for institutionalisation
• Risk factor for dementia

Risk is reduced when identified early, assessed and treated
Delirium – Aggravating Factors

- Age†
- Sensory Deprivation
- Social Isolation
- Sleep Deprivation
- Physical Restraint
- Bladder Catheter
- Adverse Events
- Polypharmacy
- Psychoactive Drugs
- Severe Illness
- Cognitive Impairment*†
- Temperature change
- Dehydration
- Low Albumin*

* Cardiac surgery
† Non-cardiac surgery

Siddiqi et al 2007
# ADVISE approach for delirium management

<table>
<thead>
<tr>
<th>Advocacy</th>
<th>Act to optimize prevention and management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diligence</td>
<td>Recognize and investigate mental status changes</td>
</tr>
<tr>
<td>Vigilance</td>
<td>Delirium patients remain vulnerable</td>
</tr>
<tr>
<td>Integration</td>
<td>Use multiple interventions and biopsychosocial approach</td>
</tr>
<tr>
<td>Support</td>
<td>Include psychotherapeutic interventions, family and staff</td>
</tr>
<tr>
<td>Education</td>
<td>Educate patients, family and staff on risks and implications</td>
</tr>
</tbody>
</table>

Weisenfeld, L. 2008
What can you do?

<table>
<thead>
<tr>
<th>Module</th>
<th>Postoperative interventions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cognitive stimulation</td>
<td>• Orientation (clock, calendar, orientation board)</td>
</tr>
<tr>
<td></td>
<td>• Avoid cognitively active medications</td>
</tr>
<tr>
<td>Improve sensory input</td>
<td>• Glasses</td>
</tr>
<tr>
<td></td>
<td>• Hearing aids/amplifiers</td>
</tr>
<tr>
<td>Mobilization</td>
<td>• Early mobilization and rehabilitation</td>
</tr>
<tr>
<td>Avoidance of psychoactive medication</td>
<td>• Elimination of unnecessary medications</td>
</tr>
<tr>
<td></td>
<td>• Pain management protocol</td>
</tr>
<tr>
<td>Fluid and nutrition</td>
<td>• Fluid management</td>
</tr>
<tr>
<td></td>
<td>• Electrolyte monitoring and repletion</td>
</tr>
<tr>
<td></td>
<td>• Adequate nutrition protocol</td>
</tr>
<tr>
<td>Avoidance of hospital complications</td>
<td>• Bowel protocol</td>
</tr>
<tr>
<td></td>
<td>• Early removal of urinary catheters</td>
</tr>
<tr>
<td></td>
<td>• Adequate central nervous system (O_2) delivery, including supplemental oxygen and transfusion for very low hematocrit</td>
</tr>
<tr>
<td></td>
<td>• Postoperative complication monitoring protocol</td>
</tr>
</tbody>
</table>

Rudolph 2011
Remember….

it’s the simple things that matter

• Pain control

• Improve sensory input – hearing aids / glasses

• Mobilise – avoid restraints

• Orientation

• Remove bladder catheters

• Sleep

• Nutrition
Delirium - Treatment

• **Treat underlying cause(s)**
  – the simple things

• **Avoid geographic relocations**

• **Antipsychotics ...**
Delirium – Pharmacological Treatment

- Antipsychotics
  - Drug of choice
    - low anticholinergic potency
    - minimal risks for hypotension
    - minimal risks for respiratory depression
Delirium – Pharmacological Treatment

• Antipsychotics
  – Haloperidol
    • Most common
  – Aripiprazole vs Haloperidol
    • Boettger et al. 2011 - retrospective case-controlled
    • Equivalent effectiveness
  – Risperidone vs Olanzapine
    • Kim et al. 2010
    • Equivalent effectiveness
<table>
<thead>
<tr>
<th>Drug</th>
<th>Treatment Class</th>
<th>Dose</th>
<th>Benefit</th>
<th>Adverse effects</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haloperidol</td>
<td>antipsychotic</td>
<td>0.25-1.0mg or IV as required for agitation</td>
<td>Relatively unsedating, few haemodynamic effects</td>
<td>EPS, esp &gt;3mg/day</td>
<td>Usually agent of choice</td>
</tr>
<tr>
<td>Olanzapine</td>
<td>Atypical antipsychotic</td>
<td>2.5-10mg daily orally, IV or IM</td>
<td>Fewer EPS than haloperid</td>
<td>More sedating than haloperid</td>
<td>Small trials</td>
</tr>
<tr>
<td>Quetiapine</td>
<td>Atypical antipsychotic</td>
<td>25-50mg</td>
<td>Fewer EPS than haloperid</td>
<td>Most sedating of atypical antipsychotics; Hypotension</td>
<td>Small trials</td>
</tr>
<tr>
<td>Risperidone</td>
<td>Atypical antipsychotic</td>
<td>0.25-1.0mg orally or IV and as required for agitation</td>
<td>Relatively nonsedating; few haemodynamic effects</td>
<td>? Slightly fewer EPS than haloperid</td>
<td>Small trials</td>
</tr>
<tr>
<td>Lorazepam</td>
<td>benzo</td>
<td>0.25-1.0mg orally or IV and as required for agitation</td>
<td>Use in sedative and alcohol withdrawal</td>
<td>Respiratory depression</td>
<td>Second line agent, except in specific cases</td>
</tr>
</tbody>
</table>

Cotton et al 2011
Delirium – Pharmacological Treatment

- **Benzdiazepines**
  - Antipsychotics contraindicated
    - Parkinson’s
    - Lewy Body dementia
    - Prior seizures
  - Maintain vigilance for paradoxical agitation†
  - May prolong or worsen course of delirium*

*Breitbart et al 1996
†Rudolph 2011
Delirium – Pharmacological Prevention

• **Maintenance of sleep-wake cycles**
  - Minimal benefit (pharmacological)
    » Aizawa 2002

• **Cognition - enhancing medications**
  - No benefit (CDP choline / donepezil)

• **Prophylactic Haloperidol**
  - No benefit
    » Kalisvaart 2005

• **Prophylactic Olanzapine**
  - Some benefit vs placebo (incidence)
  - Some detriment vs placebo (duration)
    » Cabera 2010
Other Prevention Options

- **Anaesthetic Type**
  - No benefit (GA vs Spinal) RR 1.2 (0.51 – 2.81)
    » Bergrren 1987
  - Some benefit RR 0.50
    » Parker *Cochrane* 2004

- 50% less delirium with light sedation (RCT light vs deep sedation)
  » Sieber 2010 (19% vs 40%, p=0.02)

- **Reduction in post-operative delirium**
  - Cardiac surgical patients OR 12.6 (1.05 – 112)
  - Ketamine 0.5 mg/kg at induction
Emergence
Delirium
PACU
Operative Cognitive Reserve/Comorbid Conditions
Early POCD
Late POCD
Neurotoxicity
Inflammation
Stress
Confusion
Ward/Home
Dementia
Anaesthesia
Surgery
Pre-Operative Cognitive Reserve/Comorbid Conditions
Is Delirium associated with POCD?

- Rudolph *et al* 2008
  - associated with POCD @ d7 but not 3mths

- Rudolph *et al* 2011
  - functional decline @ 1m post cardiac surgery

- Saczynski *et al* 2012
  - lower cognitive scores @ 1m & 12m post cardiac surgery

- Radke *et al* 2012
  - associated with POCD @ d7 and 3mths
  - duration predictive of POCD
  - severity predictive of POCD
ADVERSE CEREBRAL EFFECTS
OF ANÆSTHESIA ON OLD PEOPLE

P. D. Bedford
M.D. Leeds, M.R.C.P.
CONSULTANT PHYSICIAN TO THE COWLEY ROAD HOSPITAL, OXFORD

It is well established that the human brain is extremely vulnerable to short periods of vascular insufficiency (Courville 1939, Hoff et al. 1945, Corday et al. 1953). As the cerebral circulation of many elderly patients is already becoming defective (Himwich 1951), it is not surprising that the remark, "He's never been the same since his operation" is often heard in geriatric practice. It is well known, too, that in elderly people transitory

he is either quite unable to give an account of himself or gives a story upon whose accuracy no reliance can be placed. Secondly, relations and friends tend to blame any dramatic incident, such as an operation or an accident, for the dementia which has in fact been a slowly progressive intellectual degradation, antedating the operation or accident. This is a natural tendency. The old person had been suffering a mental decline so gradual as to have gone unnoticed by those with whom he lived. Defects which to an outsider would have been obvious signs of dementia had to his intimates been merely the old person's idiosyncrasies. The accident or surgical operation then necessitates his removal to hospital; and in these different surroundings (or on his return home after the interval) his oddities, foibles, and idiosyncrasies are seen afresh and in their true light as manifestations of intellectual deterioration. But he was
Neuropsychological Testing - POCD

- CERAD Word Learning Task
- Digit Symbol Substitution Test
- Trail Making Test (parts A & B)
- Controlled Oral Word Association Test (COWAT)
- Semantic Fluency Test
- Grooved Pegboard (dominant & non-dominant hands)
- National Adult Reading Test (NART)
- CogState ®
Post-Operative Cognitive Dysfunction (POCD)

• Predictors
  • age
  • education

• Impact
  • subtle changes / anecdotal reports
  • functional sequelae
  • cognitive sequelae

But...
• length of stay
• mortality

Only measured for research but documented by surgeons and anaesthetists...
Non-cardiac Surgery

Long-term postoperative cognitive dysfunction in the elderly: ISPOCD1 study

J T Moller, P Cluitmans, L S Rasmussen, P Houx, H Rasmussen, J Canet, P Rabbitt, J Jolles, K Larsen, C D Hanning, O Langeron, T Johnson, P M Lauven, P A Kristensen, A Biedler, H van Beem, O Fraidakis, J H Silverstein, J E W Beneken, J S Gravenstein, for the ISPOCD investigators*

Summary

Background Long-term postoperative cognitive dysfunction may occur in the elderly. Age may be a risk factor and hypoxaemia and arterial hypotension causative factors.

Interpretation Our findings have implications for studies of the causes of cognitive decline and, in clinical practice, for the information given to patients before surgery.


<table>
<thead>
<tr>
<th></th>
<th>Surgery n= 974</th>
<th>Control n=174</th>
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<tbody>
<tr>
<td>7 days</td>
<td>25.8%</td>
<td>3.4%</td>
</tr>
<tr>
<td>3 months</td>
<td>9.9%</td>
<td>2.8%</td>
</tr>
</tbody>
</table>
# Cardiac, Non-cardiac and Sedation

<table>
<thead>
<tr>
<th></th>
<th>Cardiac Surgery</th>
<th>Hip Replacement Surgery</th>
<th>Coronary Angiography</th>
</tr>
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<tbody>
<tr>
<td><strong>n</strong></td>
<td>312</td>
<td>162</td>
<td>152</td>
</tr>
<tr>
<td><strong>3 mths</strong></td>
<td>16% (12-21)</td>
<td>16% (11-23)</td>
<td>21% (15-28)</td>
</tr>
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</table>

Back to the future...!

Any cause which will give rise to delirium may set up a more chronic form of mental disorder quite apart from any febrile disturbance. (a) The most common form of mental disorder which comes on in such cases is of the type of acute delirious mania; (b) though such mental disorder is generally of a temporary character, it may pass into chronic weak-mindedness, or it may pass into (c) progressive dementia which cannot be distinguished from general paralysis of the insane.

To return to the first group, they are: any cause producing delirium.
Is delirium associated with dementia?

- Dementia single greatest predictor
- 3.5 times risk of developing dementia

Dementia

• 250,000 Australians have dementia

• 10 – 15 % population - Mild Cognitive Impairment (MCI)

• 95% will need 24 hour care

• cognition and function decline leading to:
  • significant cognitive impairment
  • urinary incontinence
  • pain
  • similar to cancer patients, but for much longer

• loss of appetite
• low mood
• constipation
<table>
<thead>
<tr>
<th>Informant</th>
<th>Subject</th>
</tr>
</thead>
<tbody>
<tr>
<td>Memory</td>
<td>Memory</td>
</tr>
<tr>
<td>Orientation</td>
<td>Orientation</td>
</tr>
<tr>
<td>Problem solving</td>
<td>Problem solving</td>
</tr>
<tr>
<td>Community affairs</td>
<td></td>
</tr>
<tr>
<td>Home/hobbies</td>
<td></td>
</tr>
<tr>
<td>Personal care</td>
<td></td>
</tr>
</tbody>
</table>
Dementia and Alzheimer’s Disease

• Predictors
  • age
  • education
  • MCI

• Impact
  • functional sequelae variable
  • cognitive sequelae variable

• Treatment
  • currently no effective treatment
  • prevention currently impossible
Is POCD associated with dementia?

- We don’t know yet……

Do know POCD follows anaesthesia and surgery

Does anaesthesia or surgery exacerbate conversion to dementia?
Is Anaesthesia Implicated?

Consortium Statement: First International Workshop on Anesthetics and Alzheimer’s Disease

Dmitri Baranov, MD*
Philip E. Bickler, MD, PhD†
Gregory J. Crosby, MD‡
Deborah J. Culley, MD‡
Maryellen F. Eckenhoff, PhD*
Roderic G. Eckenhoff, MD*
Kirk J. Hogan, MD, JD§
Vesna Jevovic-Todorovic, MD, PhD‖

In order to review the current status of the potential relationship between anesthesia and Alzheimer’s disease, a group of scientists recently met in Philadelphia for a full day of presentations and discussions. This special article represents a consensus view on the possible link between Alzheimer’s disease and anesthesia and the steps required to test this more definitively.


...there is sufficient evidence at multiple levels to warrant further and more definitive investigations of the onset and progression of AD and neurodegeneration after anaesthesia and surgery.
Jack et al. 2010
surgery

Years prior

Pre-surg

surgery

day 7

day 90

Years after
Jack et al. 2010
What does this mean for anaesthesia?

- 20% patients have MCI stage
- How many in the pre-clinical stage?
- Both these stages progress to AD
- What is the effect of anaesthesia and surgery?
Conclusions – Protecting the Brain

• Anaesthesia and surgery
  • Increasingly frequent
  • Delirium is common
  • Confusion is common
  • Pre-clinical AD, MCI, dementia are common
Conclusions – Protecting the Brain

What to do?

• Preoperative cognitive assessment
• Identify other risk factors
• Implement preventative strategies to reduce morbidity
• Treat delirium promptly
order. All writers and observers have noticed that it is very rarely that one cause alone is efficient for the production of any attack of insanity, and that usually there are several predisposing causes which may have been in operation for a long time, as well as one or more exciting causes which may have been in action for much shorter periods.

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