Is there a role for nutrition in psychiatric disorders?

Refeeding syndrome in anorexia nervosa

V. Haas (Germany)
The refeeding syndrome in Anorexia Nervosa

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Case report

15-year-old girl, 2.5 years history of weight loss (-20kg; dieting, exercising)
- Admission BMI 11.6 kg/m² (30 kg), ankle edema, bradycardia
- Fear of weight gain, body image distortion
- Secondary amenorrhea
- Oriented and alert, anxious, tense
- Low P (0.78 mmol/L) and glc (2.6 mmol/L), other electrolytes normal

Meal plan: 800 kcal/d orally with progressive increase incl. P, Ca, vitamins
- P remained low despite supplementation
- Day 4: fluctuating levels of consciousness, confused, slow speech
- Day 6 (1000 kcal/d): worsening of mental status; disoriented, incoherent speech, paranoid ideas, repetitive movements, agitated, aggressive, uncooperative
- Till day 13: fluctuating mental status
- Day 15: back to her normal self

¹Norris et al., Int J Eat Disord 2012;45:439-442.
The Refeeding Syndrome (RS)

**History**
- adult war or famine victims WW2
- healthy volunteers after experimental starvation (Minnesota study, 1960)
- In the 1970s following the introduction of TPN

**Definitions**
- occurrence of severe fluid & electrolyte shifts (especially, but not exclusively, of P) and their associated complications in malnourished patients undergoing refeeding
- Range of metabolic abnormalities that may accompany carbohydrate delivery in patients with severe malnutrition
- Fall in phosphate by more than 0.16 to below 0.65 or to below 0.5 mmol/L

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Metabolic consequences of the RS include:
  Key: Hypophosphataemia
  Hypokalaemia
  Hypomagnesaemia
  Fluid and sodium balance abnormalities

Pathophysiological consequences include:
  Cardiac failure
  Neuromuscular failure
  Respiratory failure
  Renal failure
  Hepatic failure
  Gastrointestinal System Failure
The Refeeding Syndrome (RS): Mechanisms\textsuperscript{6-8}

**Prolonged Fasting**
- Gluconeogenesis from lipids & protein
- Intracellular & WB minerals depleted

**Refeeding: CH load**
- on Low basal insulin
- Delayed insulin response
- Glycogen, fat & protein synthesis

Sudden move of electrolytes & fluid into intracellular space
- Hypoglycemia, hypophosphatemia

RS
Clinical features of functional electrolyte deficits
\(\uparrow\) Risk of sudden death

\textsuperscript{6}Kohn et al., Curr Opin Pediatr 2011;23:390-4. \textsuperscript{7}Mehanna et al., BMJ 2008;336:1495-8. \textsuperscript{8}Crook et al., Nutrition 2001;17:632-7.
**Occurrence**

- True incidence unknown
- AN: case reports

**Guidelines: No published RCTs of treatment, best available evidence**

10. NICE Guidelines (National Institute for Health and Clinical Excellence, CG32)

Patients at high risk of refeeding syndrome:
- Anorexia Nervosa
- Chronic alcoholism
- Oncology patients
- Postoperative patients
- Chronic malnutrition

7. Mehanna et al., BMJ 2008;336:1495-8
1. Norris et al., Int J Eat Disord 2012;45:439-442
Prevention of the RS + clinical experience

AN patient on admission: Check baseline P, K, Mg, Na, Ca, Glc and liver enzymes
↑risk if
  - Low P
  - BMI < 15, negligible intake for > 5 days
  - Purging behavior, long duration of illness

If P < 0.8 or decreases (i.e. from 1.2 to 0.9)
- Administer thiamine, multi-vitamines and trace elements
- Start feeding slowly (500 – 1000 kcal/d; 25% of estimated needs)
- Week 1: daily blood tests /electrolytes
- hydration, sodium intake
- Check vital signs, observe signs of delirium or edema
- Tube feeding gives better control
- Slowly increase feeding over 3-7 days,
- Week 2: at least 3 blood tests

Tailor to individual patient & course!
Ideal mode of supplementation not known\textsuperscript{7}

<table>
<thead>
<tr>
<th>Mineral</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phosphate</td>
<td></td>
</tr>
<tr>
<td>Maintenance requirement</td>
<td>0.3-0.6 mmol/kg/day orally</td>
</tr>
<tr>
<td>Mild hypophosphataemia (0.6-0.85 mmol/l)</td>
<td>0.3-0.6 mmol/kg/day orally</td>
</tr>
<tr>
<td>Moderate hypophosphataemia (0.3-0.6 mmol/l)</td>
<td>9 mmol infused into peripheral vein over 12 hours</td>
</tr>
<tr>
<td>Severe hypophosphataemia (&lt;0.3 mmol/l)</td>
<td>18 mmol infused into peripheral vein over 12 hours</td>
</tr>
<tr>
<td>Magnesium</td>
<td></td>
</tr>
<tr>
<td>Maintenance requirement</td>
<td>0.2 mmol/kg/day intravenously (or 0.4 mmol/kg/day orally)</td>
</tr>
<tr>
<td>Mild to moderate hypomagnesaemia (0.5-0.7 mmol/l)</td>
<td>Initially 0.5 mmol/kg/day over 24 hours intravenously, then 0.25 mmol/kg/day for 5 days intravenously</td>
</tr>
<tr>
<td>Severe hypomagnesaemia (&lt;0.5 mmol/l)</td>
<td>24 mmol over 6 hours intravenously, then as for mild to moderate hypomagnesaemia (above)</td>
</tr>
</tbody>
</table>

\textit{If signs of RS occur}\textsuperscript{1,10***}

- Immediate interruption of nutrition support
- Respiratory and cardiac care
- Resolve fluid shifts and electrolyte disorders***
- Supportive care (low stimulus environment, orientation help, family support)
- Restart nutrition with at $<50\%$ of last rate once patient is stable
- Close monitoring
Recent advances: restricting CH instead of calories

- Current protocols do not eliminate RS and result in weight loss until 2nd week
- Questionable if RS preventable by restricting calories
- Key factor: carbohydrate load and postprandial hypoglycemia
- Alternative strategy • increase cal • limit CH • maintain normal P

Modified refeeding guidelines:
(1) Continuous NG feeding at the beginning of treatment
(2) Minimum initial daily energy intake of 2000 kcal
(3) Feeds and meal plan limited to a maximum of 40% of total energy from CH
(4) Oral P 20-25 mg/kg daily in 2 doses
(5) By end of week 1: daily intake of 2700 kcal
(6) Reintroduction of oral food once medically stable
(7) Monitoring vital signs and daily blood tests during week 1 of treatment

How to achieve prolonged, steady weight gain after initial phase?

- Target: 0.5-1 kg/week
- Limited knowledge on caloric needs
- Guidelines:
  - 2200 – 2500 kcal/d sufficient for most adolescent patients\(^{13}\)
  - Individual variation between 1800 and 4500 kcal\(^{14}\)

RS is a well described but often forgotten condition
RS can be lethal
The best way to avoid it is to anticipate it
Refeeding guidelines are available:
NICE 2006
ESPEN 2005
... but they are not evidence based

A future alternative might be to target CHs instead of calories
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Thank you for your attention!

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