Insight of amnesia vs. Self awareness in Alzheimer’s disease

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ADI 04/20/ ’13
Taiwan
Dr.  What is your name?
P’ť  Mrs. Lin
Dr.  Why it is not read so on your ID ?
P’ť  They usually call me “Mrs. Lin.”

Dr.  How you know your memory is bad ?
P’ť  They always blame me for that.
H.M.: 每天都是嶄新的一天

Henry Gustav Molaison: 1926~2008
Evidence for semantic learning in profound amnesia: A study with H.M.

An unambiguous evidence that some new semantic learning can be supported by structures beyond the hippocampus proper. (O’Kane G, Kensinger EA, et al. Hippocampus 2004 14:417-425)
Braak staging of AD by Tauopathy

4                   5                    6
Time tunnel & AD: Who am I?

Onset--------Dx

x-------- Onset-------------Dx-------------------x

x-------------Onset-------------Dx-------------------x
Subjects and Methods

- Fifty-nine patients (M:F = 18:41)
- Aged 59~102, with dementia of AD
- Grouped by MMSE scores into 4:
  1. Early: >/=21, n=15
  2. Mild: 16~20, n=12
  3. Moderate: 11~15, n=19
  4. Severe: </=10, n=13
Methods

- **Self awareness** by asking each patient’s name, age, birthday and children number
- **Confrontation naming** by asking to name 3 presented objects of pencil, comb, and key
- **Insight of amnesia** by asking whether or not they have memory problems
Results

* Completed within a period of 2~3 weeks, while preparing for CT, Lab tests, and doing MMSE, CDR.

* Secondary causes of dementia, other than degenerative ones, are then excluded.
<table>
<thead>
<tr>
<th>MMSE</th>
<th>&lt;= 10 (n=13)</th>
<th>11~15 (n=19)</th>
<th>16~20 (n=12)</th>
<th>&gt;= 21 (n=15)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Awareness</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>of self</td>
<td>0/13</td>
<td>0/19</td>
<td>7/12</td>
<td>14/15</td>
</tr>
<tr>
<td>of amnesia</td>
<td>4/13</td>
<td>11/19</td>
<td>10/12</td>
<td>11/15</td>
</tr>
<tr>
<td>Naming</td>
<td>1/13</td>
<td>8/19</td>
<td>10/12</td>
<td>15/15</td>
</tr>
</tbody>
</table>

(58%)
Conclusions: 1, 2

1. Insight of amnesia in AD patients is learned.

2. The four patients in early AD, denying they had memory problems, do not learn from environmental feedbacks.
Denial of amnesia: explanation

- No trace of memory for getting aware of amnesia

- A dominant, demanding figure may preclude these 4 early AD patients from learning from feedbacks.
Conclusions: 3, 4

3. The learned insight of amnesia, through repeated reminding, stay longer than self awareness in late AD.

4. Insight of amnesia having closer test results to confrontation naming suggests that it be a cortical learning process of language.
1. Simple repeated reminding keeps the patients informed of, and oriented to, the real world day after day.

2. Reminiscence theater or TV/movie watching alone may do harm to AD patients, in some way, because of possible mis-learning.
Multiple trace theory (MTT)

* Autobiographical episodes are always mediated by the hippocampal complex.
* Some memories transform to be more semantic, can be mediated by neocortex.

(Moscovitch M et al, J. Anat. 2005;207: 35~66)
Semantic cues

- help with explicit recall in H.M. 

- Free and cued recall impaired in AD 
  (Grober E, Sanders AE et al. ADAD 2010 24:284-290)
Hypothesis of 3 different types of semantic learning

- Single, scattered semantic pearls, easily fading away, recollected by repeated reminding (AD)
- A string of semantic pearls, threaded by clues, could be recollected by cues (H.M.)
- Threaded semantic pearls making a meaningful time-hooked necklace, with hippocampus as a time filter (normals)
記憶如珠·穿索成串·鉤上成鍊
Semantic knowledge

- is gradually established through learning after birth.
- Reversely, semantic knowledge is gradually vanishing in AD patients.
- Possible slower regression by earlier intervention.
- Find the clues individually!
What are the individual clues?

- Individual clues threading the present and the past.
- Individual treatment costs a lot.
- Ineffective clues meaning “too late.”
Do something before it is too late.
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<td>5/15</td>
<td>12/21</td>
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