Late-life Mood Disorder

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大綱

- Late-life depressive disorder
  - Epidemiology
  - Presentation
  - Cognitive impairment
  - Etiologies
  - Treatment
- Late-life mania
  - Epidemiology
  - Presentation
  - Etiologies
  - Treatment

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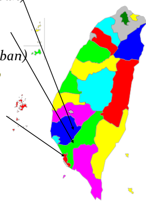
Prevalence of late-life depression in Taiwan–TOADS

- GMS-AGECAT
  - 憂鬱症 21.2%
    - 重鬱症 5.9%
    - 輕鬱症 15.3%
- DSM-IV
  - 憂鬱症 12.1%
    - 重鬱症 3.3%
    - 輕鬱症 8.8%

Nan-hwa *(rural)*
PD: 57.6
MRI: 2.97

A-lian *(semiurban)*
PD: 904.9
MRI: 9.26

Kaohsiung *(Urban)*
PD: 12878.0
MRI: 21.34



Chong et al. Brit J Psychiatry, 2001,178,25-39
Chen et al. Int J Geriatr Psychiatry, 2007, 22,557-62

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Presentation of depression in old age

- Overlap of physical and somatic psychiatric symptoms
- Minimal expression of sadness
- Somatization or disproportionate complaints associated with physical disorder
- Unexplained pain syndromes
- Neurotic symptoms of recent onset
- Deliberate self-harm (including medically trivial)
- Pseudodementia
- Depression superimposed upon dementia
- Accentuation of abnormal personality traits
- Behavior disorder
- Late onset alcohol dependency syndrome

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老年憂鬱症量表(Geriatric depression scale, GDS)

- Features
  - Avoid physical depressive symptomatology
  - Focus on cognitive aspects
- Cut-off points: 10/11
  - For physically fit group
  - Hospitalized elderly patients
  - But loses specificity in severe dementia →CSDD
- Shorter version --GDS-15
  - Item 1,2,3,4,7,8,9,10,12,14,15,17,21,22,23
  - Cut-off of 5/6 indicates depression

老年憂鬱量表

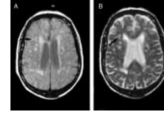
1. 基本上，您對您的生活滿意嗎？
2. 您是否減少很多的活動和興趣的事
3. 您是否覺得您的生活很空虛？
4. 您是否常常感到厭煩？
5. 您是否對將來抱有希望？
6. 您會常常煩惱一些事情，想要不去想它，卻沒有辦法嗎？
7. 您是否大部分時間精神都很好？
8. 您是否會常常害怕將有不幸的事情發生在您身上嗎？
9. 您是否大部份的時間都感到快樂？
10. 您是否常常感到無論做什麼事，都沒有用？
11. 您是否常常覺得坐立不安？
12. 您是否比較喜歡待在家裡而較不喜歡外出及不喜歡做新的事？
13. 您是否常常煩惱將來的事？
14. 您是否覺得現在有記憶力不好的困擾？
15. 您是否覺得「現在還能活著」是很好的事？

老年憂鬱量表-續

16. 您是否常常感覺心情低落、憂悶？
17. 您是否覺得您現在活得很沒有價值？
18. 您是否非常煩惱過去的事？
19. 您是否覺得生活是很快活的事？
20. 對新的工作或計劃，您是否覺得很難開始去做？
21. 您是否覺得精力很充沛？
22. 您是否感覺您現在的情況是沒有希望的？
23. 您是否覺得大部份的人都比您更幸福？
24. 您是否常常為小事情煩惱不安？
25. 您是否常常覺得想哭？
26. 您是否覺得注意力無法集中？
27. 早晨醒來，您會覺得愉快嗎？
28. 您是否覺得比較不喜歡去參加社交聚會？
29. 對日常事務，您作決定時，會比以前更困難嗎？
30. 您是否覺得現在的頭腦和往常一樣清楚？

Characteristics of late-onset depression

- Less frequent family history — Heun et al. 2001
- Higher rate of white matter hyperintensities on MRI and atherosclerosis



Greenwald et al. 1996
Lin et al. 2005
Chen et al. 2007

- More cognitive dysfunction — Chen et al. 2007
- Higher homocysteine levels — Chen et al. 2005
- Higher rate of development to dementia

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Vascular depression hypothesis

- Subtype
- Vascular risk factors, neuroimaging findings
- More cognitively impaired, more disabled, more psychomotor retardation, less insight
- Disruption by vascular lesions of striato-pallodo-thalamo-cortical pathways

- Alexopolous et al., Arch Gen Psychaitry, 1997

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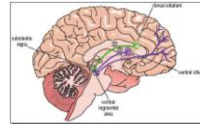
Depression-executive dysfuntion syndrome

- Depressive manifestations
  - Psychomotor retardation, reduce interest, impaired IADL
- Executive dysfunction
- Fronto-striatal dysfunction
- Poor and/or slow response to antidepressants



Alexopoulos, 2001

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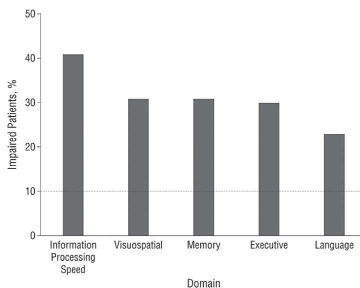
High rate of cognitive impairment in patients with late-life depression



Butters, M. A. et al. Arch Gen Psychiatry 2004;61:587-595.

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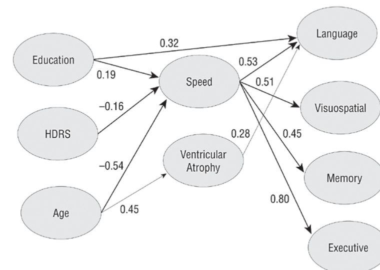
Relationships among cognitive domains and predictor variables



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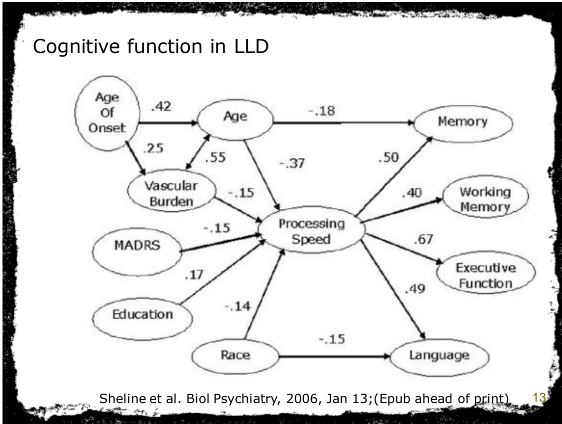

Conversion to AD from depression

- Epidemiological studies suggest
  - depression increases the risk of conversion to dementia by 2~3 fold in subjects with depression

    Bassuk, et al. Arch Gen Psychiatry 1998; 55:1073-81

    Devanand, et al. Arch Gen Psychiatry 1996; 53:175-82
- Meta-analyses study
  - OR=1.9~2.03

    Ownby, et al. Arch Gen Psychiatry 2006; 63:530-8

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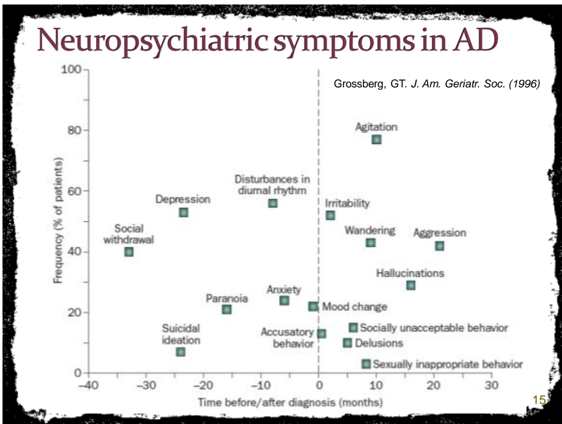

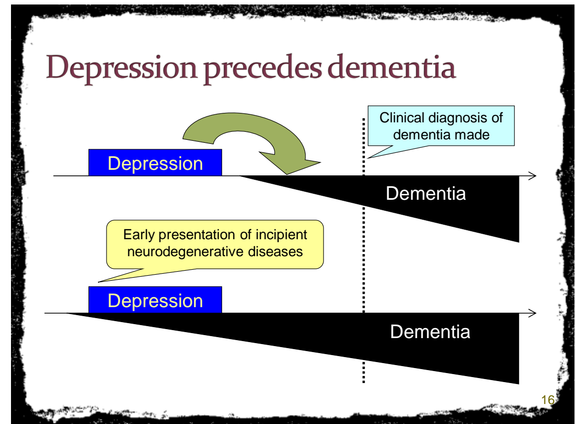

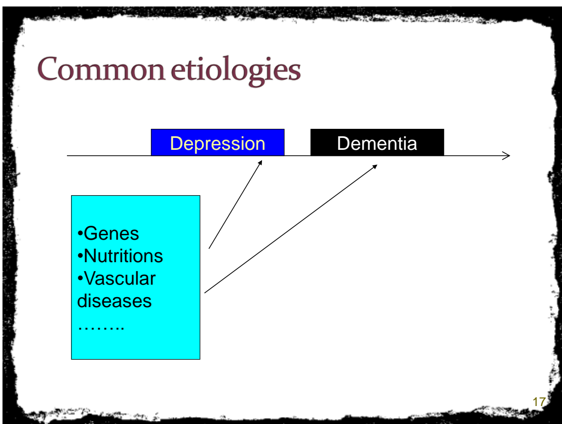

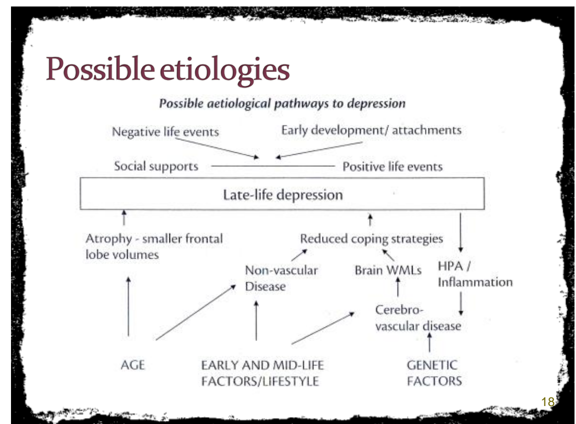

Treatment issues: Remission

- Goals of treatment
- Similar in --- compared to the younger
  - Remission rate? Response speed?
- Next step for inadequate response
  - Augmentation
  - Switching
  - Drug interactions
- Maintenance treatment

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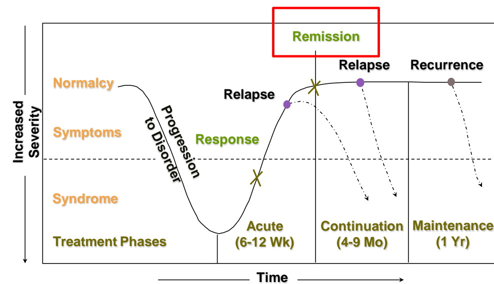
Treatment issues: 5Rs



Adapted from Kupfer DJ. *J Clin Psychiatry.* 1991;52(suppl 5):28.

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Response

- The same speed and rate as mid-life adults
  Sackeim HA, et al. Biol Psychiatry, 2006
- About 50% response rate with 1st line antidepressant
- Poor responder
  - Symptoms of anxiety
  - Medical burden
  - Cognitive impairment, ie. executive dysfunction
  Reynolds, CF, et al. IPA, 2007
- Pretreatment anxiety
  - took longer to respond to treatment
  - 2-fold higher rates of recurrence
  Andreescu C, et al. Br J Psychiatry. 2007 190:344-9

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Response and remission- a meta-analysis

- Published and unpublished trials:
  - Cochrane library, MEDLINE and meeting reports
  - 2,377 active drug vs. 1,788 placebo
- Response
  - OR=1.40 (CI=1.24-1.57)
  - Antidepressant 44.4% vs. placebo 34.7%
  - OR was higher in the 10-12 week than the 6-8 week trials (OR = 1.73 vs. 1.22)
- Remission: OR=1.27 (CI 1.12-1.44)
- ORs for discontinuation: drugs>placebo
  Nelson JC, 2008 Am J Geriatr Psychiatry, Epub ahead of print

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Next-step studies-survey of psychiatrists

- Possible options
  - Increase the dose of current antidepressants
  - Switching to another class of antidepressants
  - Switching to the same class of other antidepressants
  - Augmenting with another agents

- Mischoulon D, et al. Can J Psychiatry 2000
- Shergill SS & Katona CL. J Affect Disord 1997
- Fredman SJ, et al. J Clin Psychiatry 2000
- Nierenberg AA. J Clin Psychiatry 1991

Augmentation strategies

- Augmentation was required 53.8%
  - 3/4 inadequate treatment response & 1/4 response followed by relapse
  - 1/3 did not primarily because of consent withdrawal or comorbid medical conditions
- With augmentation (bupropion, nortriptyline, lithium)
  - Recovery rate
    - 50.0% for those with inadequate response
    - 66.7% for those with early relapse.
- Slower recovery: greater medical burden and anxiety
  Dew MA, et al. Am J Psychiatry 2007; 164:892–899

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For poor responder

- Treatment resistance LLD
  - after 3 trials of augmentation (bupropion SR, nortriptyline, and Li)
    - 60% response rate (45%--31%--43%)
    - Mean time to response: 6 wks
  - Switching to venlafaxine
    - 42% response rate
    - Mean time to response: 6.4 wks
  - Discontinuation due to side effects
    - Venlafaxine<augmentation

Whyte, EM et al. J Clin Psychiatry, 2004

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Maintenance treatment

- Recurrence rate within 2 years

	Paroxetine	Placebo
Psychotherapy	35%	68%
Clinical management	37%	58%

- Risk of placebo/paroxetine=2.4 (95% CI, 1.4-4.2)
- Monthly psychotherapy did not prevent recurrent depression

Reynolds CF, et al. NEJM, 2006

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Epidemiology of mania in old age

- A significant decrease in the community prevalence of mania at the extreme end of lifespan (1.4%→<0.1%)
  - Effectively treated?
  - High mortality?
  - "Burn out" of this disease?
- Distinct group—late onset mania
  - Cut-off age? Mostly at age of 50
  - Neurologically based manic syndrome

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Neurological co-morbidity

- Similar presentation
  - Disinhibition syndrome
  - Secondary mania
  - Pathological laughing
  - Kluver-Bucy syndrome
- High comorbid with neurological illness (4.5 fold)
  - Mostly cerebrovascular disease

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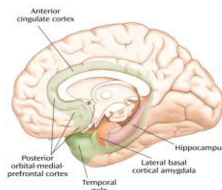
Neuroimaging of late-onset mania

- Subcortical hyperintensities
- Decreased cerebral blood flow
- Silent cerebral infarctions



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Clinical course and outcome

- Course
  - First episode: depressive episode
  - Mean of latency to mania: 15yrs
  - Cerebral-organic changes & comorbid neurological disorders
  - Most experience both depressive and manic episodes
- Outcome
  - High rates of mortality and morbidity

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Li Tx

- Used with considerable caution: kidney function
- Acute treatment with 300-600 mg/d
- Maintenance therapy: 0.5mmol/l or more
- Drug interaction
  - Thiazide diruretics
  - Angiotensin-converting enzyme (ACE) inhibitors
  - NSAID
  - ...

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Others Tx

- Valproic acid
  - A very reasonable alternative mood stablizer
  - Well tolerated
  - 1000-1500mg daily
- Carbamazepine
  - Highly neurotoxic
  - Serum level: <9ug/ml
  - Drug interaction issue
- Atypical antipsychotics
  - Monotherapy or adjunctive therapy
  - Metabolic side effects, CVA risk

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謝謝收看 敬請指教

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