Behavioral problems in neurological disorders

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- **Dementia**
- Stroke
- Epilepsy
- Parkinson disease

Definition of BPSD

- Symptoms of disturbed perception, thought content, mood or behavior that frequently occur in patients with dementia
- Umbrella term for a heterogeneous group of non-cognitive symptoms that are almost ubiquitous in dementia

IPA BPSD Educational Pack-Module 1

Classification of BPSD

Psychological symptoms	*Behavioral symptoms*
Delusion	Aggression
Hallucination	Wandering
Paranoia	Sleep disturbance
Depression	Inappropriate eating disord.
Anxiety	Inappropriate sexual beh.
Reduplication	
Misidentification	

Luxenberg JS. Clinical issues in the BPSD of dementia. Int J Geriatr Psychiatry. 2000;15:S5-S8

Change of BPSD as *progression*

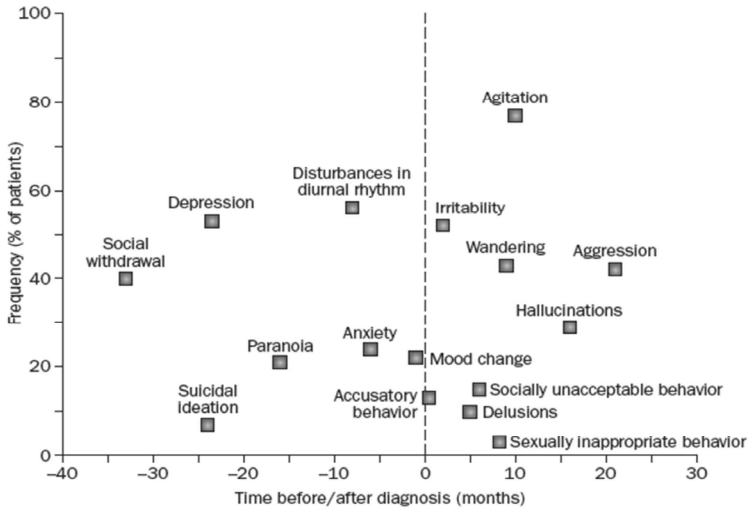
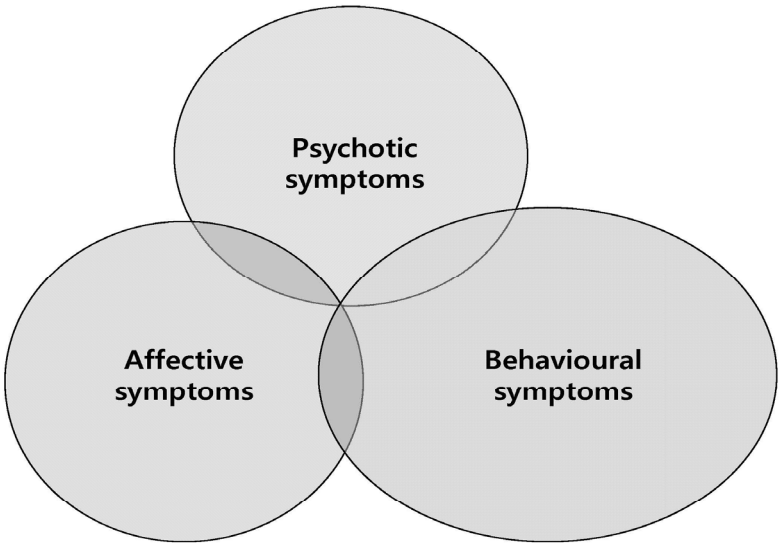


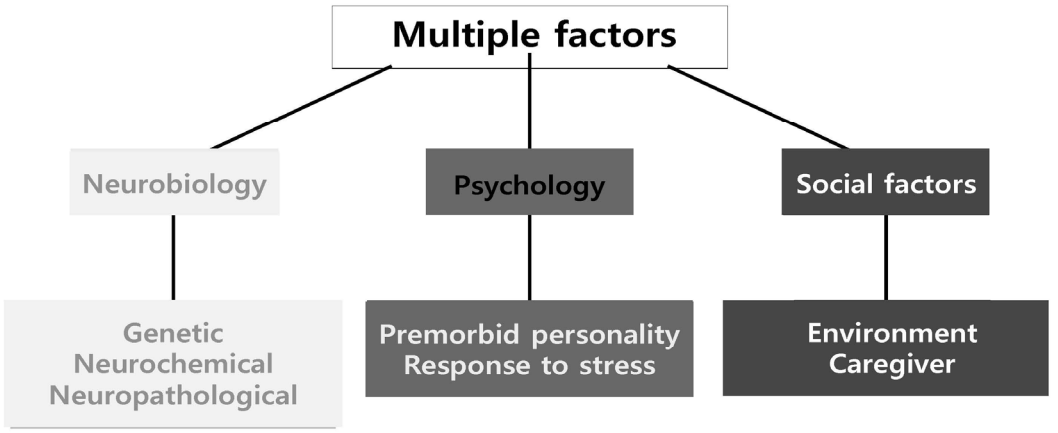
Figure 1 | Peak frequency of behavioral symptoms as Alzheimer disease progresses. Permission obtained from Blackwell Publishing © Jost, B. C. & Grossberg, G. T. *J. Am. Geriatr. Soc.* **44**, 1078–1081 (1996).

Nat. Rev. Neurol. 2009; 5: 245-255

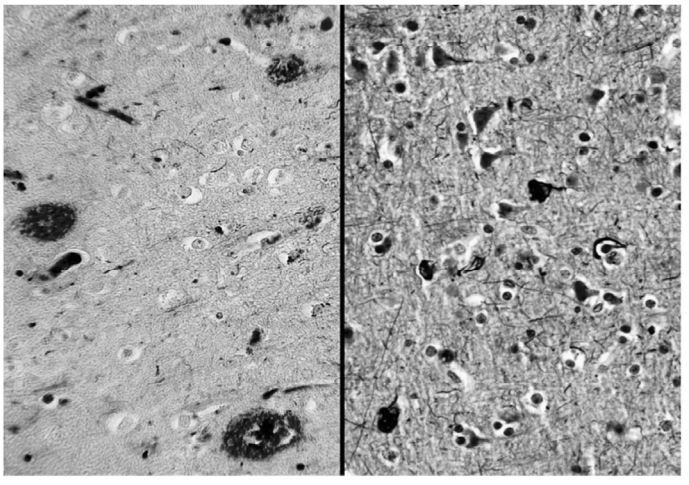
The Spectrum of BPSD



Multiple Causes of BPSD



Lawlor BA. Int Psychogeriatr 1996



Without agitation /With agitation

Agitated and psychotic patients have
Neurofibrillary tangles in the frontal cortex

Tekin et al, Ann Neurol 2001; 49: 355–361

NPI

- Delusion
- Hallucination
- Agitation/Aggression
- Depression/Dysphoria
- Anxiety
- Euphoria/Elation
- Apathy/Indifference
- Disinhibition
- Irritability/Lability
- Aberrant motor behavior
- Sleep/Night-time behavior
- Appetite/Eating change

Delusion

NPI

Types of delusion

- 다른 사람이 해치려고 한다.
- 물건을 훔쳐간다.
- 배우자가 바람을 피운다.
- 모르는 사람이 자기 집에 살고 있다.
- 배우자나 가족을 다른 사람으로 믿고 있다.
- 자기 집을 다른 사람의 집이라고 믿고 있다.
- 가족들이 자기를 버린다.
- TV나 잡지의 등장인물이 현재 집에 있는 것으로 믿고 있다.
- 기타 비정상적인 믿음이 있다.

가. 망상 (Delusions)

사실이 아닌 것을 사실이라고 믿습니까?
예를 들어 자기를 해치려고 한다든가, 무엇을 훔쳐 갔다고 주장합니까?
또는 가족을 다른 사람이라고 믿거나 자기집을 자기집이 아니라고
믿습니까?

아니오 (다음 선별질문으로) (예)(아래의 세부 질문으로)

1. 다른 사람이 환자분을 해치려 한다고 믿습니까? ( )
2. 다른 사람들이 물건을 훔쳐 갔다고 믿고 있습니까? (O)
3. 배우자가 바람을 피운다고 믿고 있습니까? (O)
4. 모르는 사람이 자기 집에 살고 있다고 믿습니까? ( )
5. 배우자나 가족을 다른 사람이라고 믿고 있습니까? ( )
6. 자기 집을 다른 사람의 집으로 믿고 있습니까? (O)
7. TV나 잡지의 등장 인물을 현재 집에 있는 것으로 믿고 있습니까?( )

빈도

1. 드물다 - 일주일에 1회 미만
2. 가끔 - 일주일에 1회 정도
3. 자주 - 일주일에 몇번 그러나 매일은 아님
4. 매우 자주 - 하루에 한번 이상

정도

1. 경함 2. 보통 3. 심함

보호자 고통 정도

0. 고통이 전혀 없다 1. 고통이 매우 적다
2. 고통이 경한 편이다 3. 고통이 보통이다
4. 고통이 심한 편이다 5. 고통이 매우 심하다

Delusion as 4 subtypes

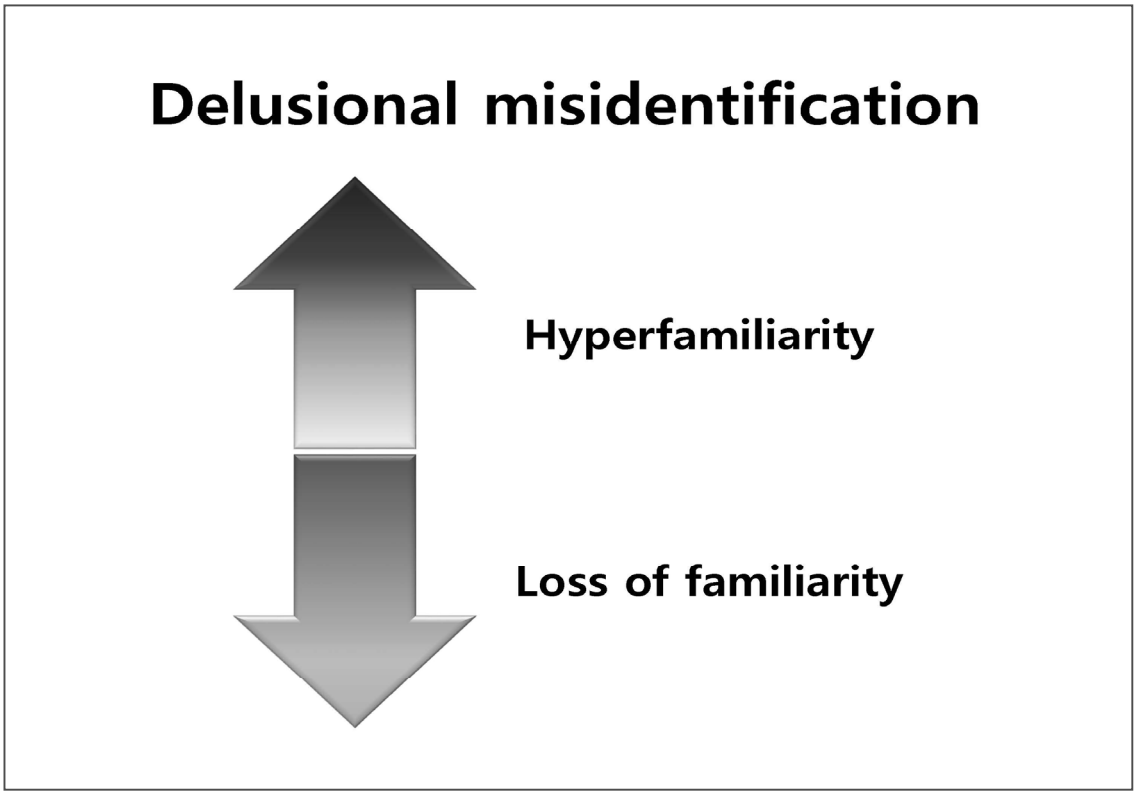
- **Paranoid delusion**
  (persecutory, theft, infidelity, abandonment et al)
- **Misidentification delusion**
  (Capgras, phantom boarder, reduplication place, TV sign, Mirror sign et al)
- **Expansive delusion**
  (erotic, grandeur et al)
- **Mixed delusion**

Perez-Madriñan G Alzheimer disease with psychosis: excess cognitive impairment is restricted to the misidentification subtype. *Am J Geriatr Psychiatry* 2004 ;12:449-456.

Delusional misidentification

- **Definition**
  - Misperception of external stimuli with an associated belief or elaboration that is held with delusional intensity
- **Types**
  - Phantom border
  - This is not my home
  - Delusional misidentification of mirror images
  - Delusional misidentification of TV images
  - Misidentification of other person
    Capgra syndrome
    Fregoli syndrome
    Intermetamorphosis
    Subjective double
    Reverse Subjective Syndrome

Ballard CG, O'Brien J, James I, Swann A: Dementia: management of BPSD. 2001; 17-33
Cummings JL, Mega MS. Neuropsychiatry & behavioral neuroscience. 2003;172-186



Delusional reduplication-misidentification

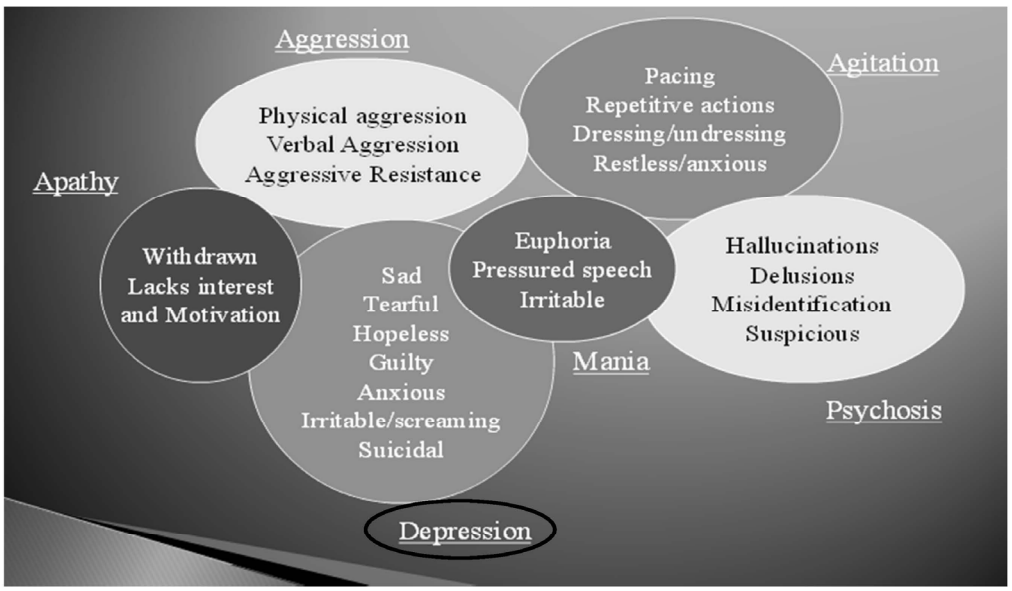
Neurology® 2010;74:970-974

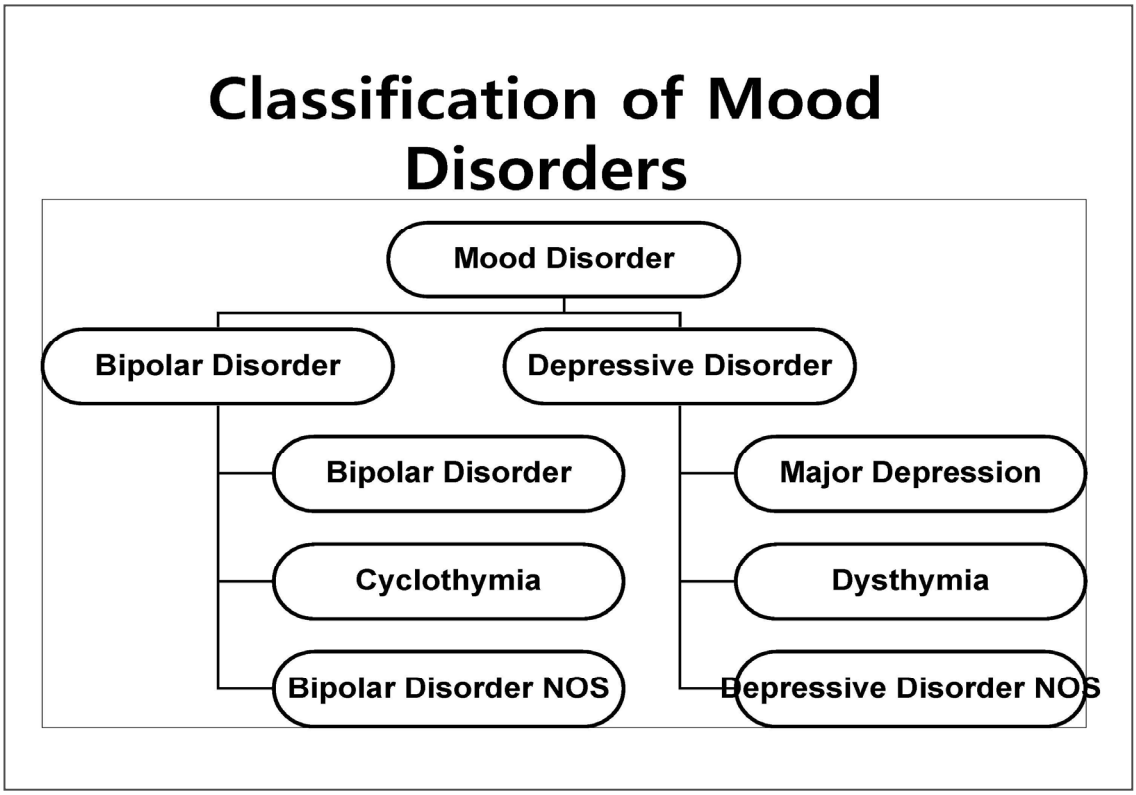
Loss of familiarity		
People		
Capgras[3,5,6,13,14,20-22]	Familiar persons are impostors or have doubles with different psychic identity	No autonomic response to familiar faces despite conscious recognition (converse of prosopagnosia)
Mirror sign (self-misidentification)[23,24]	Misidentification of oneself in the mirror	Able to identify others in the mirror
Places		
Foreign reduplicative paramnesia (Capgras for places)[25]	Familiar place such as home is considered a duplicate in another location	Sometimes labeled reduplicative paramnesia
Disorientation for place[26]	A familiar place exists in another location	New York Hospital is in Manhattan but Manhattan is in Boston
Hyperfamiliarity		
People		
Fregoli[6,14,22,30]	A stranger is believed to be a familiar person	A person takes on others' appearances but retains psychic identity; often persecutes patient
Intermetamorphosis[22]	Familiar or unfamiliar people change both physical and mental identity	Usually transforms into someone familiar to the patient
Subjective doubles[22]	Familiar or unfamiliar person is mentally and physically transformed into the patient	The patient considers this other person a double
Places		
Reduplicative paramnesia[27-29]	A place simultaneously exists in two or more physical locations	For example, a strange hospital is duplicated in a hometown setting

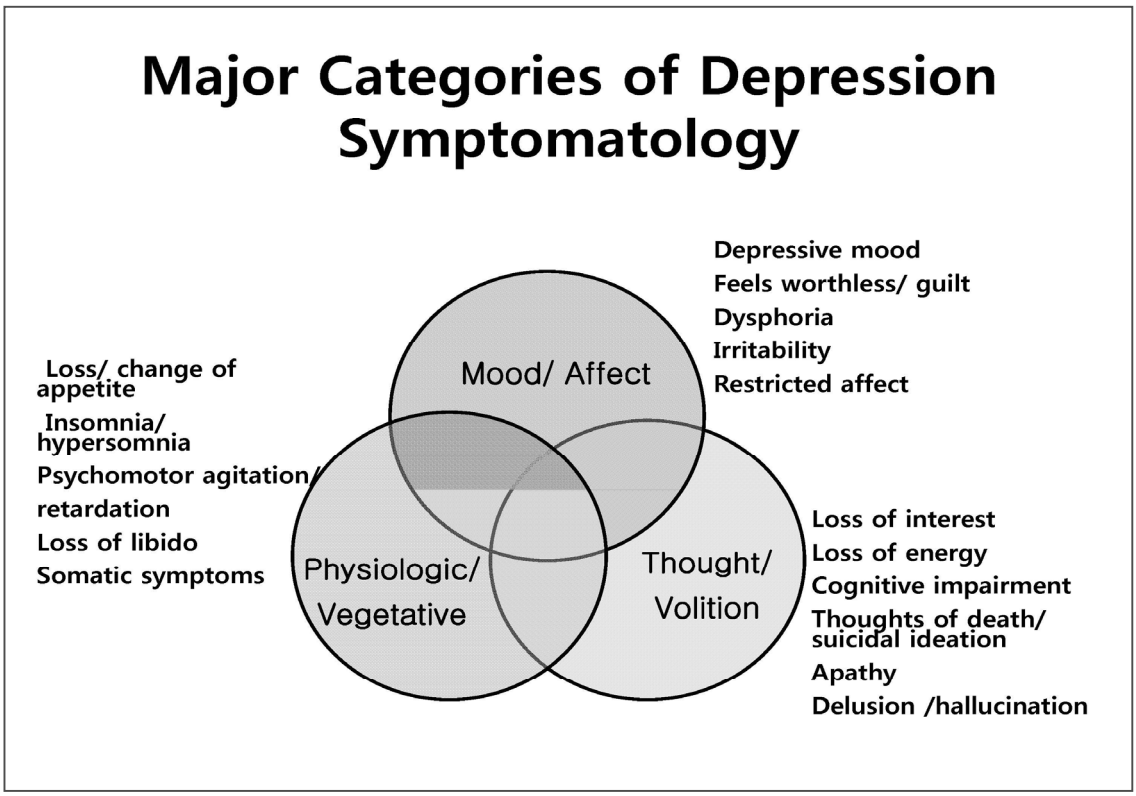
Depression

- ***NPI***
  - 슬퍼서 눈물을 흘린다.
  - 슬프거나 기분이 처진 것처럼 행동하거나 믿는다.
  - 자신이 실패자라고 말하거나, 자기 자신을 과소 평가한다.
  - 자신이 나쁜 사람이라고 이야기 하거나 벌받아 마땅하다고 생각.
  - 매우 낙심한 것처럼 보이거나 자기에게 미래가 없다고 말한다.
  - 자신이 없으면 다른 가족들이 더 잘 지낼 것이라고 말한다.
  - 죽고 싶다고 말하거나 자살하겠다는 이야기를 한 적이 있다.
  - 그밖에 우울해 하거나 슬퍼하는 증상이 있다.

BPSD Symptom Clusters




Classification of Mood Disorders
Mood Disorder
Bipolar Disorder
Depressive Disorder
Bipolar Disorder
Cyclothymia
Bipolar Disorder NOS
Major Depression
Dysthymia
Depressive Disorder NOS


Major Categories of Depression Symptomatology
Depressive mood
Feels worthless/ guilt
Dysphoria
Irritability
Restricted affect
Mood/ Affect
Loss/ change of appetite
Insomnia/ hypersomnia
Psychomotor agitation/ retardation
Loss of libido
Somatic symptoms
Physiologic/ Vegetative
Thought/ Volition
Loss of interest
Loss of energy
Cognitive impairment
Thoughts of death/ suicidal ideation
Apathy
Delusion /hallucination

Major Depressive Episode: DSM-IV

> 5 including 1 or 2, > 2 weeks

1. ***Depressed mood***
2. ***Loss of interest***
3. Loss or change of appetite
4. Insomnia/ hypersomnia
5. Psychomotor agitation/ retardation
6. Loss of energy
7. Feeling of worthlessness/ guilt
8. Cognitive impairment
9. Recurrent thoughts of death/ suicidal ideation

Diagnostic criteria for Major Depressive Episode:(DSM-5)

A. **Five (or more)** of the following symptoms have been present during the same 2- week period and represent a change from previous functioning; at least one of the symptoms is either (1) depressed mood or (2) loss of interest or pleasure.

Note: Do not include symptoms that are clearly due to a general medical condition, or mood-incongruent delusions or hallucinations.

1. **Depressed mood** most of the day, nearly every day, as indicated by either subjective report (e.g., feels sad or empty) or observation made by others (e.g., appears tearful). Note: In children and adolescents, can be irritable mood.
2. **Markedly diminished interest or pleasure** in all, or almost all, activities most of the day, nearly every day (as indicated by either subjective account or observation made by others).
3. **Significant weight lo**ss when not dieting or weight gain (e.g., a change of more than 5 percent of body weight in a month), or decrease or increase in appetite nearly every day. Note: In children, consider failure to make expected weight gains.
4. **Insomnia or hypersomnia** nearly every day.
5. **Psychomotor agitation or retardation** nearly every day (observable by others, not merely subjective feelings of restlessness or being slowed down).
6. **Fatigue or loss of energy** nearly every day.
7. Feelings of worthlessness or excessive or inappropriate **guilt** (which may be delusional) nearly every day (not merely self-reproach or guilt about being sick).
8. **Diminished ability to think or concentrate**, or indecisiveness, nearly every day (either by subjective account or as observed by others).
9. Recurrent thoughts of **death** (not just fear of dying), recurrent suicidal ideation without a specific plan, or a suicide attempt or a specific plan for committing suicide.

B. The symptoms cause clinically **significant distress or impairment** in social, occupational or other important areas of functioning.

C. The symptoms are not due to the direct physiological effects of a substance (e.g., a drug of abuse, a medication) or a general medical condition (e.g., hypothyroidism).

Cornell Scale for Depression in Dementia

※ 지난 1주일 간 환자가 보인 증상을 평가하시오.	
평가방법/ 평가기간:지난 1주일, 평가기준: 0=없었음, 1=경도 또는 간헐적, 2=중증 또는 자주, 9=평가 불능	
1. 불안 (불안한 표정, 불안감 표현, 반복적 고민, 지나친 걱정 등)	◎ ① ② ⑨
2. 슬픔 (슬픈 표정, 슬픈 감정 표현, 서글픈 목소리, 눈물을 흘리거나 글썽거림, 등)	◎ ① ② ⑨
3. 즐거운 일에 대한 반응 소실	◎ ① ② ⑨
4. 과민 (쉽게 신경질을 냄, 참을성이 없음)	◎ ① ② ⑨
5. 초조 (가만히 있지 못함. 손을 쥐어 짬, 머리카락을 뜯는 모습 등)	◎ ① ② ⑨
6. 지체 (느린 행동, 느린 말소리, 반응 지연, 등)	◎ ① ② ⑨
7. 다양한 신체 증상 호소 (소화기 증상만 호소하는 경우 0으로 평가)	◎ ① ② ⑨
8. 흥미상실 (일상 활동에 참여하지 않으려고 함, 최근 일 개월 이내에 갑작스럽게 발생한 경우에만 점수를 부여함)	◎ ① ② ⑨
9. 식욕 저하 (평소에 비해 적게 먹음)	◎ ① ② ⑨
10. 체중 감소 (지난 1개월간 2Kg 이상의 감소가 있을 경우 2로 평가)	◎ ① ② ⑨
11. 활력 상실 (쉽게 피로함, 지속적으로 활동을 할 수 없음; 최근 일 개월 이내에 갑작스럽게 발생한 경우에만 점수를 부여함)	◎ ① ② ⑨
12. 하루를 주기로 기분이 변하며, 아침에 증상이 심해짐.	◎ ① ② ⑨
13. 잠들기 힘듬 (평상시보다 늦게 잠 듬)	◎ ① ② ⑨
14. 수면 도중 자주 깸	◎ ① ② ⑨
15. 너무 일찍 깸 (평상 시보다 아침에 일찍 깸)	◎ ① ② ⑨
16. 자살 사고 (삶이 가치 없다고 느낌, 자살에 대한 바램, 자살기도, 등)	◎ ① ② ⑨
17. 자존심 저하(자신을 책망, 자신이 가치 없다고 생각, 실패했다는 생각, 등)	◎ ① ② ⑨
18. 비관 (가장 나쁜 쪽으로 전망, 희망이 없다고 생각 등)	◎ ① ② ⑨
19. 기분에 일치되는 망상 (병에 걸리거나, 망하거나, 다 잃어버릴 것이라는 망상)	◎ ① ② ⑨
총 점	**/38점**

CSDD
: 환자와 보호자와 인터뷰를 시행하며 작성

Reliability and Validity of the Korean Version of CSDD in Dementia

- A cut-off score of 7 for the CSDD-K
  : sensitivity - 87.5%, specificity - 100%.

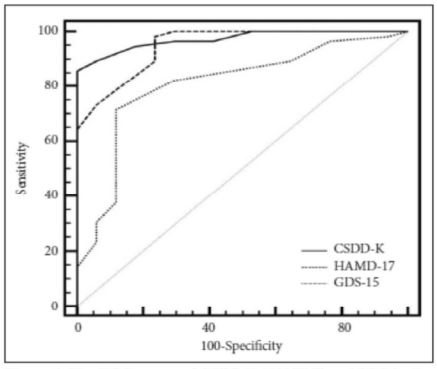


Figure 1. The ROC curves of CSDD-K, HAMD17 and GDS for the prediction of the diagnosis of depression in AD. ROC: Receiver Operation Characteristics, CSDD-K: Korean version of Cornell Scale for Depression in Dementia, $HAMD_{17}$: 17-item Hamilton Depression Rating Scale, GDS_{15}: 15-item Geriatric Depression Scale, AD: Alzheimer's disease.

<Lim HK et al. Psychiatry Investig 2012;9(4):332-8>

Geriatric Depression Scale

Geriatric Depression Scale (GDS-15)

Development of the Korean version of the Geriatric depression scale and its short form among elderly psychiatric patients, *J Psychosom Res 2004:57:297-305*		
1	당신은 평소 자신의 생활에 만족합니까?	예/아니오
2	당신은 활동과 흥미가 많이 저하되었습니까?	예/아니오
3	당신은 앞날에 대해서 희망적입니까?	예/아니오
4	당신은 대부분의 시간을 맑은 정신으로 지냅니까?	예/아니오
5	당신은 대부분의 시간이 행복하다고 느끼십니까?	예/아니오
6	당신은 지금 살아있다는 것이 아름답다고 생각합니까?	예/아니오
7	당신은 가끔 낙담하고 우울하다고 느낍니까?	예/아니오
8	당신은 지금 자신의 인생이 매우 가치가 없다고 느끼십니까?	예/아니오
9	당신은 인생이 매우 흥미롭다고 느끼십니까?	예/아니오
10	당신은 활력이 충만하다고 느끼십니까?	예/아니오
11	당신은 자주 사소한 일에 마음의 동요를 느끼십니까?	예/아니오
12	당신은 자주 울고 싶다고 느낍니까?	예/아니오
13	당신은 아침에 일어나는 것이 즐겁습니까?	예/아니오
14	당신은 결정을 내리는 것이 수월합니까?	예/아니오
15	당신의 마음은 이전처럼 편안합니까?	예/아니오

Original GDS
: Yesavage et al.(1983)
•30문항
•>11 depression
•11~20: mild depression
•21~30:moderate depression

GDS-15문항
5점이하: 정상
6~9: 중등도 우울증상
10이상: 우울증

Causes of BPSD

- Intellectural and cognitive changes
  - Amnesia, agnosia, apraxia, aphasia, apathy
- Neurotransmitter dysfunction
  - Dopamine, serotonin, cholinergic, adrenergic, GABA
- Instinctual behaviors under stress
  - Territoriality
  - defensiveness

Print ISSN 1738-1495 / On-line ISSN 2384-0757
Dement Neurocogn Disord 2016;15(2):37-42 / http://dx.doi.org/10.12779/dnd.2016.15.2.37

DND

ORIGINAL ARTICLE

The Neuropsychological Characteristics in Early Stage of Alzheimer's Patients with Depression

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Background and Purpose Although depression is a common psychiatric symptom in Alzheimer's disease (AD), there has not been a lot of research on neuropsychological characteristics of this symptom. To determine the characteristic neuropsychological deficit in patients with depression compared to patients without depression, this study compared each neuropsychological test between AD patients with depression and without depression.

Methods Psychotropic-naïve (drug-naïve) early stage [Clinical Dementia Rating Scale (CDR)=0.5 or CDR=1] probable AD patients with depression (n=77) and without depression (n=179) were assessed with the Seoul Neuropsychological Screening Battery, which includes measures of memory, intelligence, and executive functioning.

Results AD patients with depression had lower scores on the digit forward, digit backward, calculation, and Color Word Stroop Test tests compared to AD patients without depression.

Conclusions Our study showed that AD patients with depression have disproportionate cognitive deficit, suggesting frontal (especially in the left dorsolateral), left hemisphere and left parietal dysfunction. Considering the neuropsychological differences between AD patients with depression and without depression, depression may have specific anatomic substrates.

Table 2. A comparison of neuropsychological tests between AD patients without depression and with depression

	Depression (-)	Depression (+)	p-value*
Digit forward	5.15±1.38	4.61±1.24	0.005
Digit backward	3.21±1.17	2.63±0.66	0.000
K-BNT	31.89±10.83	30.46±11.18	0.362
Calculation	9.49±3.24	7.94±3.44	0.001
Ideomotor praxis	3.65±1.62	3.42±1.57	0.321
SVLT immediate recall	12.90±4.77	12.30±4.35	0.359
SVLT delayed recall	1.68±2.56	1.58±2.21	0.763
RCFT copy	24.32±9.49	21.75±9.15	0.076
RCFT immediate copy	5.08±5.61	4.42±3.84	0.413
RCFT delayed copy	4.44±5.42	3.74±4.14	0.379
Contrasting	16.96±6.08	16.68±6.04	0.751
Go-no-go	14.02±6.80	13.16±6.80	0.394
Fist-edge-arm	2.08±0.94	2.00±1.18	0.678
Alternating hand	2.30±0.93	2.21±1.15	0.618
Alternating square	1.53±1.32	1.47±1.65	0.433
Luria	1.52±1.32	1.61±1.75	0.800
COWAT animal	10.26±3.71	9.70±3.71	0.262
COWAT supermarket	10.35±5.08	9.63±5.25	0.327
COWAT phonemic	16.43±8.40	14.26±8.42	0.165
CWST word correct	106.66±14.37	96.67±21.28	0.003
CWST color correct	52.95±26.70	40.58±23.72	0.033

*Independent t-test was performed.
AD: Alzheimer's disease, COWAT: Controlled Oral Word Association Test, CWST: Color Word Stroop Test, K-BNT: Korean version of the Boston Naming Test, RCFT: Rey-Osterrieth Complex Figure Test, SVLT: Seoul Verbal Learning Test.

Table 3. Correlation between GDS15 and specific neuropsycological tests in AD patients with depression

	Correlation coefficient	p-value*
Digit forward	-0.159	0.013
Digit backward	-0.237	0.000
K-BNT	-0.059	0.368
Calculation	-0.229	0.000
Ideomotor praxis	-0.030	0.642
SVLT immediate recall	-0.122	0.058
SVLT delayed recall	-0.033	0.668
RCFT copy	-0.118	0.084
RCFT immediate copy	-0.046	0.503
RCFT delayed copy	-0.005	0.937
Contrasting	-0.070	0.287
Go-no-go	-0.064	0.331
Fist-edge-arm	-0.012	0.887
Alternating hand	-0.117	0.331
Alternating square	-0.021	0.797
Luria	0.069	0.381
COWAT animal	-0.097	0.131
COWAT supermarket	-0.117	0.069
COWAT phonemic	-0.138	0.075
CWST word correct	-0.308	0.000
CWST color correct	-0.215	0.023

*Pearson bivariate correlation was performed.
AD: Alzheimer's disease, COWAT: Controlled Oral Word Association Test, CWST: Color Word Stroop Test, GDS15: Geriatric Depression Scale 15, K-BNT: Korean version of the Boston Naming Test, RCFT: Rey-Osterrieth Complex Figure Test, SVLT: Seoul Verbal Learning Test.

Print ISSN 1738-1495 / On-line ISSN 2384-0757
Dement Neurocogn Disord 2016;15(2):37-42 / http://dx.doi.org/10.12779/dnd.2016.15.2.37

DND

ORIGINAL ARTICLE

The Neuropsychological Characteristics in Early Stage of Alzheimer's Patients with Depression

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Background and Purpose Although depression is a common psychiatric symptom in Alzheimer's disease (AD), there has not been a lot of research on neuropsychological characteristics of this symptom. To determine the characteristic neuropsychological deficit in patients with depression compared to patients without depression, this study compared each neuropsychological test between AD patients with depression and without depression.
Methods Psychotropic-naïve (drug-naïve) early stage [Clinical Dementia Rating Scale (CDR)=0.5 or CDR=1] probable AD patients with depression (n=77) and without depression (n=179) were assessed with the Seoul Neuropsychological Screening Battery, which includes measures of memory, intelligence, and executive functioning.
Results AD patients with depression had lower scores on the digit forward, digit backward, calculation, and Color Word Stroop Test tests compared to AD patients without depression.
Conclusions Our study showed that AD patients with depression have disproportionate cognitive deficit, suggesting frontal (especially in the left dorsolateral), left hemisphere and left parietal dysfunction. Considering the neuropsychological differences between AD patients with depression and without depression, depression may have specific anatomic substrates.

Dementia and Neurocognitive Disorders
2012; 11: 87-94

■ ORIGINAL ARTICLE ■

Clinical Characteristics of Behavioral and Psychological Symptoms in Patients with Drug-naïve Alzheimer's Disease

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Background: Behavioral and psychological symptoms of dementia (BPSD) are less well-defined aspects of Alzheimer's disease (AD). We designed this study to explore the followings: 1) the clinical profiles of BPSD 2) the clustered-groups domains of the Korean-Neuropsychiatric Inventory (K-NPI) assessment of BPSD 3) the clinical characteristics of the clustered-groups of BPSD in patients with drug-naïve probable AD. **Methods:** Descriptive and cluster analyses of the 12 K-NPI domains were done in 220 patients with drug-naïve probable AD. After clustering these domains, characteristics of these positive symptoms clustered-group of patients were compared with the negative symptoms groups of patients. **Results:** The mean Korean-Mini Mental Status Examination (K-MMSE), Clinical Dementia Rating (CDR) scale, and K-NPI scores were 15.0, 1.6, and 14.2, respectively. The CDR and K-MMSE scores correlated with total K- NPI scores, and depression was the most common symptom. According to cluster analysis, five major clusters were identified. Using the associated neuropsychological dysfunctions, characteristics of each group were defined. **Conclusions:** This study identified the clustered-domains for K-NPI, and suggested the possible anatomical substrates for these groups in drug-naïve AD patients. These attempts may clarify the complex and bizarre behavioral and psychological symptoms as more neurologically relevant symptoms.

Key Words: *Behavioral and psychological symptoms of dementia, Drug-naïve, Alzheimer's disease, Cluster analysis*

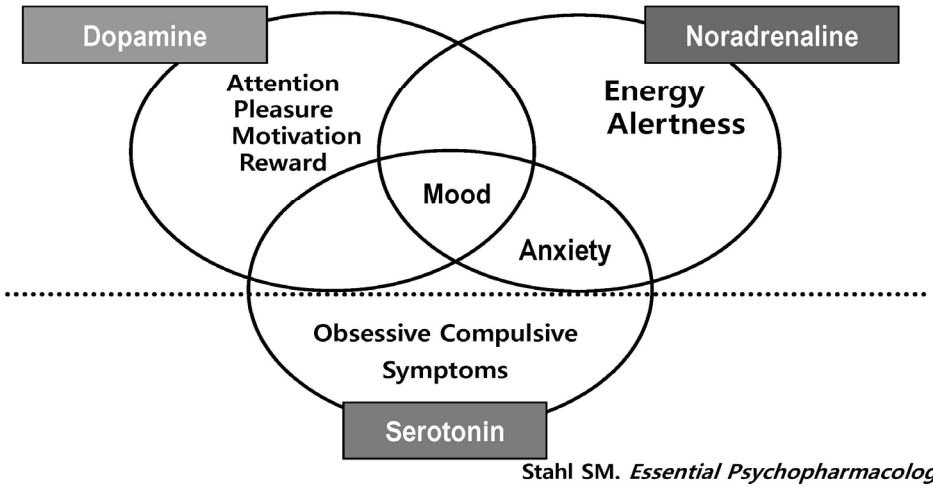
BPSD that will not respond to medication

- Wandering
- Inappropriate urination/ defecation
- Inappropriate dressing/ undressing
- Annoying repetitive activities (perseveration) or vocalization
- Hiding/ hoarding
- Eating inedibles
- Tugging at/ removal of restraints
- Pushing wheelchair bound co-residents

Antidepressants in Depression

- In general,
  - Clinical improvement : 60~70% (cf. Placebo 30%)
  - Onset of antidepressant effects : several weeks
  - All antidepressants act on 5-HT or NE system, some on DA
  - Similar efficacy, different safety and side effect profiles
  - Side effects are related with action on various neurotransmitter system

Neurotransmitter Regulation of Mood, Cognition, and Behavior



Stahl SM. *Essential Psychopharmacology. 1996.*
Foote SI. *Psychopharmacology.* 1995.

Classification		Drugs
TCA	Tricyclic Antidepressants	Amitryptiline / Clomipramine / Imipramine / Desipramine / Nortriptyline
MAOI	Monoamine Oxidase Inhibitor	Phenelzine / Isocarboxazid
RIMA	Reversible inhibitor of MAO-A	Moclobemide
SSRI	Selective Serotonin Reuptake Inhibitor	Fluoxetine / Fluvoxamine / Paroxetine / Sertraline / Citalopram / Escitalopram
SARI	Serotonin Antagonist/Reuptake Inhibitor	Trazodone / Nefazodone
SPARI	Serotonin Partial Agonist/Reuptake Inhibitor	Vilazodone
SNRI	Serotonin Norepinephrine Reuptake Inhibitor	Venlafaxine / Desvenlafaxine / Duloxetine / Milnacipran
NRI	(Selective) Norepinephrine Reuptake Inhibitor	Reboxetine / Evidoxetine / Atomexetine
NaSSA	Noradrenergic and specific serotonergic antidepressant	Mirtazapine / Mianserin
NDRI	Norepinephrine Dopamine Reuptake Inhibitor	Bupropion
SNDRI	Serotonin-Norepinephrine-Dopamine Reuptake Inhibitor	Amitifadine
New ATDs	Melatonergic Antidepressant	Agomelatine
	Serotonin Modulator and Stimulator	Vortioxetine
	NMDA Blockade	Ketamine? Dextromethorphan?
Herbal ATDs	Herbal Antidepressant	St. John's wort ext.

Table 2. **Commonly Used Antidepressants for Major Depression.***

Medication	Starting Dose	Therapeutic Dose	Half-Life†	Side Effects	Comments
SSRIs				Nausea, dyspepsia, anorexia, tremors, anxiety, sexual dysfunction, jitteriness, insomnia, hyponatremia‡	Risk of serotonin syndrome if combined with certain drugs§
Fluoxetine (Prozac)¶	10 mg once daily	10–60 mg once daily	Long		
Sertraline (Zoloft)¶	25 mg once daily	50–200 mg once daily	Short	Loose stools, diarrhea	
Citalopram (Celexa)¶	10 mg once daily	20–60 mg once daily	Short		Relatively few drug–drug interactions
Escitalopram (Lexapro)	10 mg once daily	10–30 mg once daily	Short		Relatively few drug–drug interactions
Paroxetine (Paxil)¶	10 mg once daily	20–50 mg once daily	Short	Dry mouth, drowsiness, fatigue, weight gain, hyponatremia‡	
SNRIs				Nausea, sweating, dry mouth, dizziness, agitation, insomnia, somnolence, sexual dysfunction	Relatively few drug–drug interactions, risk of serotonin syndrome if combined with certain drugs§
Venlafaxine (Effexor)¶	25 mg once daily	25–150 mg twice daily	Ultrashort	Hypertension	
Venlafaxine XR (Effexor XR)	37.5 mg once daily	75–300 mg once daily	Short	Hypertension	
Duloxetine (Cymbalta)	30 mg once daily	20–60 mg once daily	Short		Should not be broken (enteric coated)
Other newer antidepressants					
Mirtazapine (Remeron)¶	15 mg every night	15–45 mg every night	Short	Sedation, weight gain, no sexual side effects	Relatively few drug–drug interactions
Bupropion (Wellbutrin)¶	75 mg once daily	75–150 mg twice or thrice daily	Ultrashort	Insomnia, agitation, jitteriness; no sexual side effects or weight gain	Contraindicated in patients at increased risk for seizures
Bupropion SR (Wellbutrin SR)	100 mg once daily	100–150 mg twice daily	Short	Insomnia, agitation, jitteriness; no sexual side effects or weight gain	Contraindicated in patients at increased risk for seizures
Tricyclic antidepressants‖				Sedation, weight gain, dry mouth, urinary retention, constipation, blurry vision, orthostatic hypotension, impairment of cardiac conduction	
Nortriptyline (Pamelor)¶	10 mg every night	75–125 mg every night	Short	Fatigue	
Desipramine (Norpramin)¶	25 mg once daily	100–200 mg once daily	Short	Insomnia, agitation	

종류	시작용량(mg)	사용범위(mg)
Nortriptyline	10-20	10-50(25-100)
Trazodone	12.5-25	25-200(50-150)
Fluoxetine	10	10-40(20-60)
Sertraline	25	50-200
Paroxetine	10	10-40
Citalopram	10	10-40
Venlafaxine	12.5	200
Mirtazapine	7.5	15-30
Nafazodone	50	50-200

양영순, 한일우 치매의 행동 심리 증상의 치료 대한치매학회 교과서

종류	시작용량(mg)	사용범위(mg)
Midazolam	2.5	5-15
Lorazepam	0.5	0.5-4
Alprazolam	0.25	0.25-2
Clonazepam	0.125	0.25-2

양영순, 한일우 치매의 행동 심리 증상의 치료 대한치매학회 교과서

Aggression/Agitation

- ***NPI***
  - 환자를 도와주려고 할 때 화를 낸 적이 있느냐? 목욕이나 옷을 갈아 입힐 때 저항한 적이 있느냐?
  - 고집을 부리느냐? 자기 방식대로 하려고 하느냐?
  - 비협조적이냐?
  - 다루기 힘들게 하는 행동이 있느냐?
  - 소리를 지르거나 욕을 할 때가 있느냐?
  - 문을 세게 닫거나 발로 차거나 물건을 던지느냐?
  - 남을 헤치거나 때리려고 하느냐?
  - 다른 공격적 행동 혹은 안절부절 못하는 행동이 있느냐? (Original version: Others _____)

Aggression/Agitation

- ***Subtypes of agitation*** (Cohen-Mansfield & Billing)

Physically non-aggressive
- · general restlessness
- · repetitive mannerism
- · pacing
- · hiding things

Physically aggressive
- · hitting
- · pushing
- · scratching
- · kicking or biting

Verbally non-aggressive
- · negativism
- · constant request for attention
- · verbal bossiness
- · complaining or whining

Verbally aggressive
- · screaming
- · cursing
- · temper outburst
- · making strange noise

Ballard CG, O'Brien J, James I, Swann A: Dementia: management of BPSD. 2001; 61-78

anger in neurologic disease

Man must evolve for all human conflict a method which rejects revenge, aggression and retaliation. The foundation of such a method is love.
- Martin Luther King Jr. (1929 – 1968)

- Anger에 대한 명확한 정의는 어려움 (수백가지의 사전적 의미)
- Anger, rage, aggression, hostility 등 수많은 유사한 개념이 존재
- 모호한 정의(inaccurate definition) 와 대체사용 (used interchangeably) 은 결국 혼란을 야기
- **Anger** vs **aggression** vs **hostility**

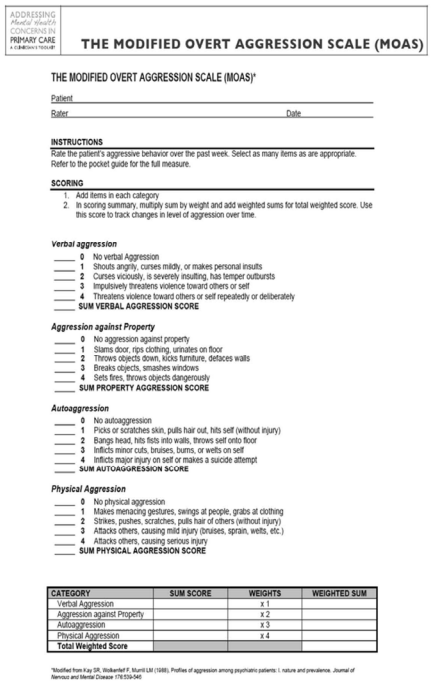
	Definitions	Dimension
Anger	**Emotional reaction** of feeling that varies in intensity, from mild irritation to fury and rage *(Spielberger CD, 1988)*	Emotion
	A constellation of specific uncomfortable subjective experiences and associated cognitions that have variously associated verbal, facial, bodily, and automatic reactions *(DiGiuseppe and Tafrate, 2007)*	
Aggression	**Behavior** intended to harm another *(Baron & Richardson,1994)*	Behavior
	Hostile, threatening, and violent behaviors *(Onyike and Lyketsos, 2011)*	
Hostility	An **attitude** of resentment, suspiciousness, and bitterness coupled with the desire to get revenge or to have destructive goals for ones anger *(Endler and Hunt, 1968)*	Attitude (cognitive component)
	A **negative attitude** toward one or more people that is reflected in a decidedly unfavorable judgment of the target (*Berkowitz,1993)*	

State-Trait Anger Expression Inventory (STAXI)

- **Spielberger**에 의해 개발되었으며 **self-reporting 방식**으로서 현재는 **STAXI-2** 개발됨
- 한국형은 청소년 집단 대상 (12 ~ 18세)으로 표준화 연구되었으며 타당도 및 신뢰도 높은 편
- 44 items (STAXI-2는 57 items), 0점 (전혀 아니다) ~ 4점 (아주 그렇다)
- Anger attack questionnaire, Cook-Medley hostility scale, Buss-Durkee hostility scale 등과 비교하였을 때 **anger expression을 측정**할 수 있다는 점에서 차별성

Modified Overt Aggression Scale (MOAS)

- **Behavior rating scale**으로서 4가지 타입의 aggressive behavior를 평가
  - Verbal aggression
  - Aggression against property
  - Autoaggression
  - physical aggression
- **매우 간단하며 소요시간이 짧은 것이 장점**
- 선별검사로 개발되었으나 **추적검사**에도 널리 사용
- **특히 TBI를 가진 환자에게서 유용**
- 타당도 및 신뢰도 높은 편



ADDRESSING Mental Health CONCERNS IN PRIMARY CARE

THE MODIFIED OVERT AGGRESSION SCALE (MOAS)

THE MODIFIED OVERT AGGRESSION SCALE (MOAS)*

Patient

Rater Date

INSTRUCTIONS

Rate the patient's aggressive behavior over the past week. Select as many items as are appropriate. Refer to the pocket guide for the full measure.

SCORING

1. Add items in each category
2. In scoring summary, multiply sum by weight and add weighted sums for total weighted score. Use this score to track changes in level of aggression over time.

Verbal aggression

____ 0 No verbal Aggression
____ 1 Shouts angrily, curses mildly, or makes personal insults
____ 2 Curses viciously, is severely insulting, has temper outbursts
____ 3 Impulsively threatens violence toward others or self
____ 4 Threatens violence toward others or self repeatedly or deliberately
____ SUM VERBAL AGGRESSION SCORE

Aggression against Property

____ 0 No aggression against property
____ 1 Slams door, rips clothing, urinates on floor
____ 2 Throws objects down, kicks furniture, defaces walls
____ 3 Breaks objects, smashes windows
____ 4 Sets fires, throws objects dangerously
____ SUM PROPERTY AGGRESSION SCORE

Autoaggression

____ 0 No autoaggression
____ 1 Picks or scratches skin, pulls hair out, hits self (without injury)
____ 2 Bangs head, hits fists into walls, throws self onto floor
____ 3 Inflicts minor cuts, bruises, burns, or welts on self
____ 4 Inflicts major injury on self or makes a suicide attempt
____ SUM AUTOAGGRESSION SCORE

Physical Aggression

____ 0 No physical aggression
____ 1 Makes menacing gestures, swings at people, grabs at clothing
____ 2 Strikes, pushes, scratches, pulls hair of others (without injury)
____ 3 Attacks others, causing mild injury (bruises, sprain, welts, etc.)
____ 4 Attacks others, causing serious injury
____ SUM PHYSICAL AGGRESSION SCORE

CATEGORY	SUM SCORE	WEIGHTS	WEIGHTED SUM
Verbal Aggression		x 1	
Aggression against Property		x 2	
Autoaggression		x 3	
Physical Aggression		x 4	
Total Weighted Score			

*Modified from Kay SR, Wolkenfeld F, Murrill LM (1988). Profiles of aggression among psychiatric patients: I. nature and prevalence. Journal of Nervous and Mental Disease 176:559-546

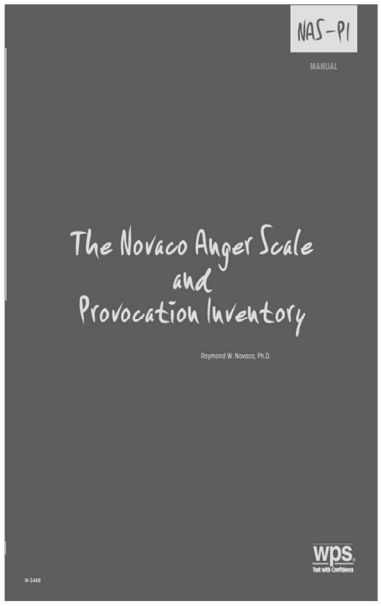
Novaco Anger Scale and Provocation Inventory (NAS-PI)

- 타당도 및 신뢰도 높은 편
- NAS는 전문기관 (anger-management services)의 표본과 비임상적인 표본을 비교했을 때에도 정확도가 높은 편 (*Jones, Thomas-Peter, & Trout, 1999)*

NAS-PI Scores

Novaco Anger Scale
- Cognitive (COG)
- Arousal (ARO)
- Behavior (BEH)
- Anger Regulation (REG)
- NAS Total

Provocation Inventory
- PI Total



Aggression treatments

✓ Nonpharmacological intervention

- Individual therapies
- Classical psychoanalysis
- Insight oriented psychotherapy
- Cognitive - behavior therapy
- Supportive psychotherapy
- Behavior modification
- Multisystem therapy
- Group therapies

✓ Pharmacological interventions

- Antipsychotics
  - Typical/Atypical
- Lithium
- Antiepileptic drugs
  - With/without mood stabilizing qualities
- Antidepressant
- Beta blockers
- Antiandrogenic therapy

JoS
JOURNAL OF STROKE

Journal of Stroke 2016;18(3):244-255
http://dx.doi.org/10.5853/jos.2016.01144

Review

Post-stroke Mood and Emotional Disturbances: Pharmacological Therapy Based on Mechanisms

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Post-stroke mood and emotional disturbances are frequent and diverse in their manifestations. Out of the many post-stroke disturbances, post-stroke depression, post-stroke anxiety, post-stroke emotional incontinence, post-stroke anger proneness, and post-stroke fatigue are frequent and important symptoms. These symptoms are distressing for both the patients and their caregivers, and negatively influence the patient's quality of life. Unfortunately, these emotional disturbances are not apparent and are therefore often unnoticed by busy clinicians. Their phenomenology, predicting factors, and pathophysiology have been under-studied, and are under-recognized. In addition, well-designed clinical trials regarding these symptoms are rare. Fortunately, these mood and emotional disturbances may be treated or prevented by various methods, including pharmacological therapy. To administer the appropriate therapy, we have to understand the phenomenology and the similarities and differences in the pathophysiological mechanisms associated with these emotional symptoms. This narrative review will describe some of the most common or relevant post-stroke mood and emotional disturbances. The phenomenology, factors or predictors, and relevant lesion locations will be described, and pharmacological treatment of these emotional disturbances will be discussed based on presumable pathophysiological mechanisms.

Keywords Stroke; Depression; Emotion; Serotonin; Treatment

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Received: August 18, 2016
Revised: September 7, 2016
Accepted: September 8, 2016

This study was supported by a grant from the Ministry for Health, Welfare and Family Affairs, Republic of Korea (HI14C1985).

The authors have no financial conflicts of interest.

Movement Disorders
Vol. 23, No. 2, 2008, pp. 195–199

Anger in Parkinson's Disease: A Case-Control Study

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Abstract: Cognitive-psychiatric features of Parkinson's disease (PD) are common and they may be as disabling as the motor features of the disease. PD has been associated with stoic and inflexible personality traits. While many features of personality have been studied in PD, a systematic study of anger trait and anger expression in PD has not been performed. We used the Spanish adapted version of the state–trait anger Expression Inventory-2 (STAXI-2), comprised of six scales and an anger expression index, to measure anger trait and anger expression. There were 126 PD patients with depressive symptoms and 126 age- and gender-matched controls. PD patients had lower levels of state anger (15.8 ± 3.1 vs. 17.9 ± 5.3, $P < 0.001$), trait anger (19.2 ± 5.3 vs. 20.7 ± 6.0, $P < 0.05$), anger expression-out (9.0 ± 2.5 vs. 10.5 ± 3.0, $P < 0.001$), and anger expression index (26.1 ± 8.8 vs. 29.6 ± 9.4, $P = 0.002$); and higher levels in anger expression-in (14.0 ± 3.4 vs. 12.2 ± 3.2, $P < 0.001$), anger control-out (18.6 ± 5.0 vs. 16.1 ± 5.0, $P < 0.001$), and anger control-in (14.3 ± 4.7 vs. 13.0 ± 4.5, $P < 0.05$) than controls. These differences persisted in analyses adjusting for age, gender, and depressive symptoms. Conclusions: PD patients showed lower levels of external expression of anger and higher levels of control of anger. Our results demonstrate another dimension to the stoic personality trait seen in PD. © 2007 Movement Disorder Society

Key words: Parkinson's disease; non-motor features; psychiatric.

Disinhibition

- ***NPI***
  - 충동적인 행동을 한다.
  - 전혀 모르는 사람에게 마치 잘 알고 있는 것처럼 말을 건넨다.
  - 상대방의 기분을 고려하지 않고 말하거나, 감정을 상하게 하는 말을 한다.
  - 과거와 달리 저질스러운 이야기나 성적 이야기를 한다.
  - 개인적 문제나 사적인 문제를 공공연하게 이야기 한다.
  - 평소 성격과는 달리 제멋대로 행동하거나 남을 만지거나 안으려는 등의 행동을 한다.
  - 그 밖의 충동조절을 못하는 행동

Disinhibition

- ***Manifestation***
  - Features of reminiscent of hypomania
    - Overactivity
    - Inattentiveness; Distractibility; Restlessness
    - Unproductive rushing from one activity to another;
    - Marked lack of persistence
  - Features of social disinhibition
    - Inappropriate jocularity
    - Disinhibited & social inappropriateness
    - Intrusiveness
    - Impulsivity
    - Sexual disinhibition

IPA BPSD Educational Pack-Module 2
Ames D, Burns A, O'Brian J. Dementia 4th ed. (2010)

Aberrant motor behavior

- ***NPI***
  - 특별한 목적 없이 집안에서 왔다 갔다 한다.
  - 장롱이나 서랍을 뒤지는 일이 다.
  - 반복적으로 옷을 입었다 벗었다 한다.
  - 단추를 풀었다 채웠다 하거나 무언가를 계속 만지작 거리거나 실을 감는 것 같은 반복적인 행동을 한다.
  - 지나치게 안절부절 못하는 경향이 있다. 가만히 앉아 있지 못하고 발을 구르거나 반복적으로 손가락을 두드린다.
  - 그밖에 반복행동이 있다.

Wandering
(Definitions)

- **Early Definitions**
  - Aimless or purposeless walking
  - Increased amount of walking

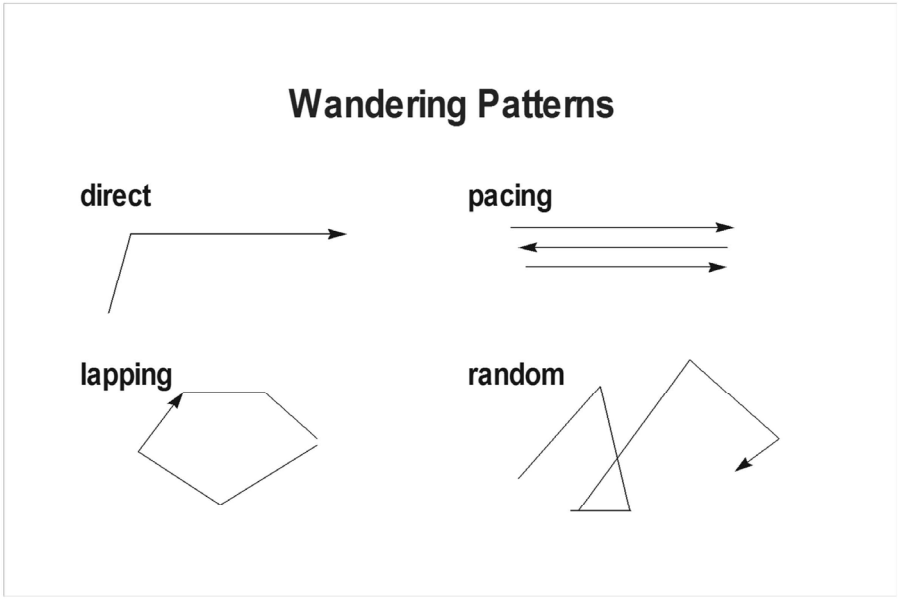
Snyder et al., 1978
Monsour& Robb, 1982

- **NANDA Definition**

- Meandering, aimless, or repetitive locomotion that exposes a person to harm and frequently is incongruent with boundaries, limits, or obstacles

NANDA, 1999

Wandering as Spatial or Geographic Patterns



Clozapine 사용지침

1. 12.5-25mg의 저용량으로 시작하며, 30일에 걸쳐 1일 100mg 정도가 될 때까지 서서히 증량한다

2. 혈중 백혈구 수치를 모니터 하면서 다음과 같은 원칙을 따르도록 한다
   - 2-1. 백혈구 수치가 3,500/mm^3 이하일 경우, 투약하지 않는다.
   - 2-2. 백혈구 수치가 3,000-3500/mm^3 사이일 경우, 1주일에 2번 백혈구 및 감별혈구계산을 시행한다.
   - 2-3. 백혈구 수치가 3,000/mm^3 이하로 감소할 경우, 일단 투약을 중단하고 환자를 모니터 한다.
   - 2-4. 백혈구 수치가 2,000/mm^3 이하로 감소할 경우, 치료를 중단하고 clozapine을 재시도 하지 않는다.
   - 2-5. 백혈구 수치가 지난번 검사 수치보다 30% 정도 감소했을 경우, 검사를 다시 해 본다. 재검사에서도 의미있을 정도로 감소되어 있을 경우, 전문가에게 자문을 구한다.
   - 2-6. 치료 시작 후 백혈구 수치가 점진적으로 감소하는 경우, 지속적으로 모니터 하면서 상기 언급된 대로 시행한다.

양영순, 한일우 치매의 행동 심리 증상의 치료 대한치매학회 교과서

BPSD Usually Not Amenable to Antipsychotics

• wandering	• vocally disruptive behaviour	• inappropriate voiding
• hiding and hoarding	• inappropriate dressing /undressing	• eating inedible objects
• repetitive activity	• tugging at seatbelts	• pushing wheel chair bound residents

Note: Try to avoid use of antipsychotics if possible for residents with dementia due to Parkinson's disease or Lewy Body dementia. Cholinesterase inhibitors are the first line of treatment for residents with psychosis and aggression associated with these type of dementias. Cholinesterase inhibitor drugs are covered by the Ministry of Health through the Alzheimer Drug Therapy Initiative.