BEST PRACTICES FOR MEDICATION MANAGEMENT OF DEMENTIA-RELATED BEHAVIORS

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Disclosures

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no disclosures

Off-label use of medications

will be discussed

GLOSSARY

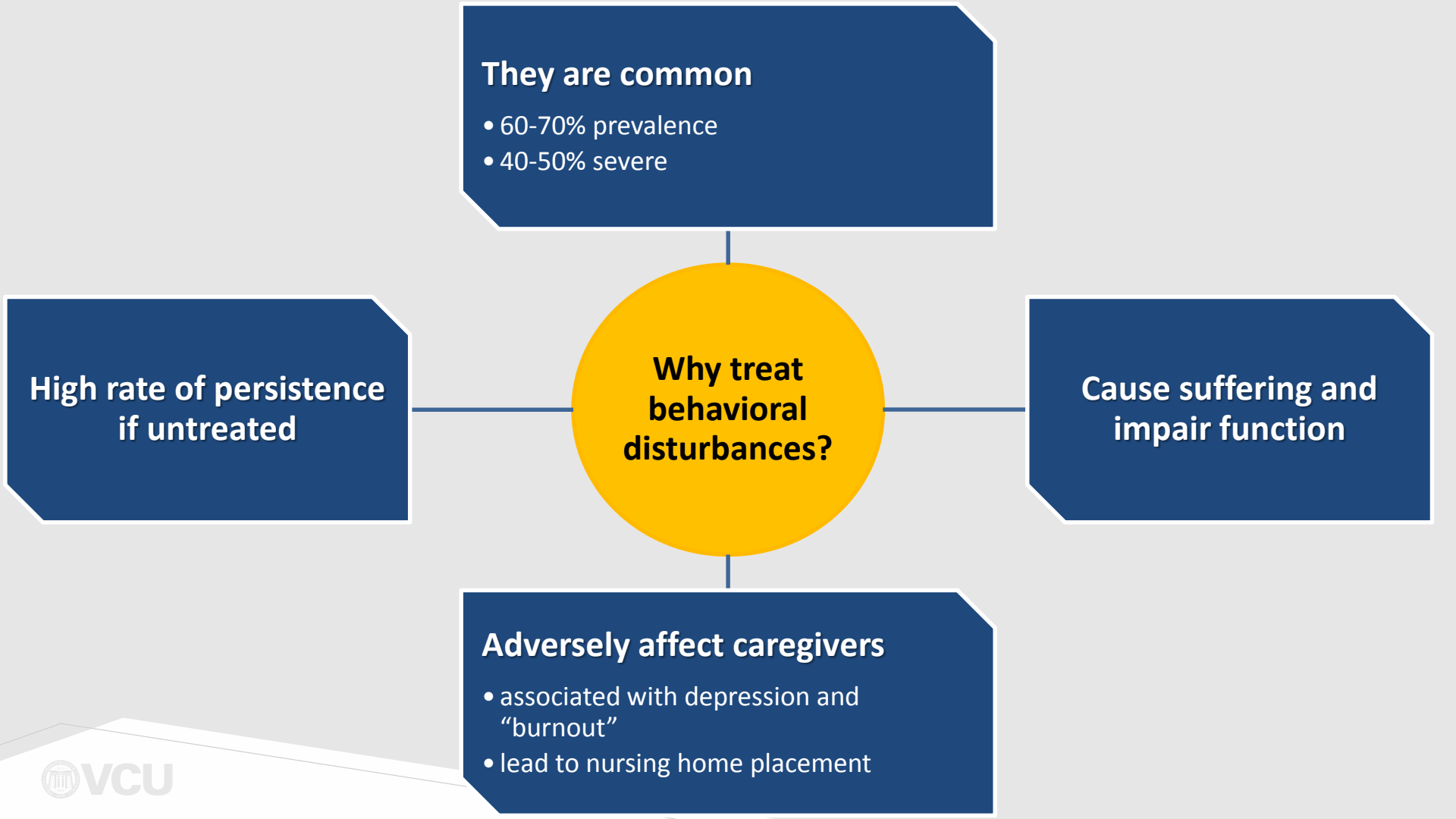
Anhedonia	inability to feel pleasure
bid	Seen on a prescription, it is an abbreviation for "bis in die" which in Latin means twice a day. *(Similarly, tid = three times a day)*
Chorea	Abnormal involuntary movement disorder, one of a group of neurological disorders called dyskinesias. The term **chorea** is derived from the Greek word χορεία (=dance; see choreia), as the quick movements of the feet or hands are comparable to dancing.
Dysarthria	Dysarthria is a condition in which the muscles you use for speech are weak or you have difficulty controlling them. Dysarthria often is characterized by slurred or slow speech that can be difficult to understand.
MMSE	Mini–Mental State Examination (**MMSE**) or Folstein test is a 30-point questionnaire that is used extensively in clinical and research settings to measure cognitive impairment. It is commonly used in medicine and allied health to screen for dementia.
SSRI	Selective serotonin re-uptake inhibitors or serotonin-specific reuptake inhibitors are a class of drugs that are typically used as antidepressants in the treatment of major depressive disorder and anxiety disorders.
DSM	Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition is the 2013 update to the American Psychiatric Association's classification and diagnostic tool

Psychological symptoms and behavioral abnormalities are common and prominent characteristics of dementia.

They include symptoms such as depression, anxiety psychosis, agitation, aggression, disinhibition, and sleep disturbances.

Approximately 30% to 90% of patients with dementia suffer from such behavioral disorders.

Behavioral disturbances in dementia


They are common
• 60-70% prevalence
• 40-50% severe
High rate of persistence if untreated
Why treat behavioral disturbances?
Cause suffering and impair function
Adversely affect caregivers
• associated with depression and "burnout"
• lead to nursing home placement

Four Stage Process

1.Observation

2.Diagnosis

3.Treatment

4.Evaluation

1. OBSERVATION

Need to place the behavior in context

Careful history from patient and caregiver

- onset
- course
- circumstances
- environment

Careful examination

- physical
- neurological
- mental status

Laboratory studies as indicated

- electrolytes
- CBC
- urinalysis
- imaging

2. DIAGNOSIS

Look for specific syndromes where possible

- depression
- mania
- delirium
- apathy

Mental state can drive behavior

- delusions
- hallucinations

Disruptions of drive

- sexuality
- sleeping
- eating

Abnormal reaction to environment

- catastrophic reaction
- adjustment disorder

3. TREATMENT

Remove specific cause

Treat specific syndromes

Manage non-specific problems

- consider non-pharmacologic interventions first
- choose target symptoms
- distinguish treatment from sedation
- go back to see if treatment is still needed

4. EVALUATION

Revisit target symptoms

Look for side effects

- always consider delirium
- consider akathisia

Evaluate the success of the treatment

- it helps to agree in advance

Have a back-up plan

- can be helpful to share this with families

1. OBSERVATION

- **Need to place the behavior in context**
- **Careful history from patient and caregiver**
  - onset, course, circumstances, environment
- **Careful examination**
  - physical, neurological, mental status
- **Laboratory studies as indicated**
  - electrolytes, CBC, urinalysis, imaging

2. DIAGNOSIS

- **Look for specific syndromes where possible**
  - depression, mania, delirium, apathy
- **Mental state can drive behavior**
  - delusions, hallucinations
- **Disruptions of drive**
  - sexuality, sleeping, eating
- **Abnormal reaction to environment**
  - catastrophic reaction, adjustment disorder

3. TREATMENT

- **Remove specific cause**
- **Treat specific syndromes**
- **Manage non-specific problems**
  - consider non-pharmacologic interventions first
  - choose target symptoms
  - distinguish treatment from sedation
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4. EVALUATION

- **Revisit target symptoms**
- **Look for side effects**
  - always consider delirium
  - consider akathisia
- **Evaluate the success of the treatment**
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Some common categories of behavioral disturbances are:

MOOD DISORDERS

(e.g., depression, apathy, euphoria);

AGITATION

(pacing, wandering, sexual disinhibition, aggression).

SLEEP DISORDERS

(insomnia, hypersomnia, night-day reversal);

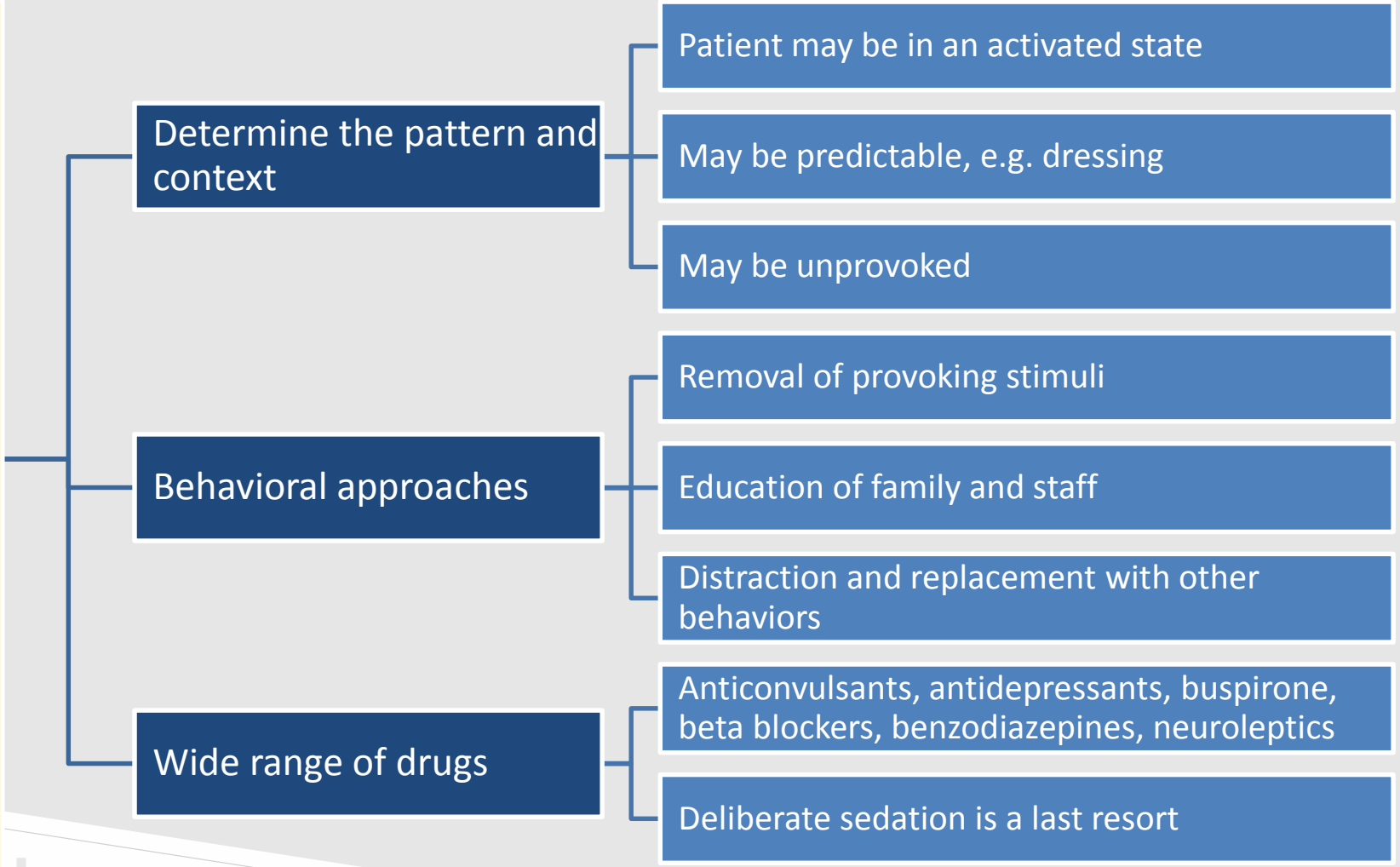
PSYCHOTIC SYMPTOMS

(delusions and hallucinations); and

DEPRESSION

- High prevalence
  ~15-25% in Alzheimer's disease
- Sadness, anhedonia, vital sense, self-attitude
- Presentation may be atypical
  - patients may lack descriptive ability
  - agitation, weight loss, tearfulness
  - consider prior, family history precipitants
- Treatment requires persistence
  - 6-8 weeks at adequate dose

AGGRESSION


Determine the pattern and context
Patient may be in an activated state
May be predictable, e.g. dressing
May be unprovoked
Behavioral approaches
Removal of provoking stimuli
Education of family and staff
Distraction and replacement with other behaviors
Wide range of drugs
Anticonvulsants, antidepressants, buspirone, beta blockers, benzodiazepines, neuroleptics
Deliberate sedation is a last resort

PSYCHOSIS

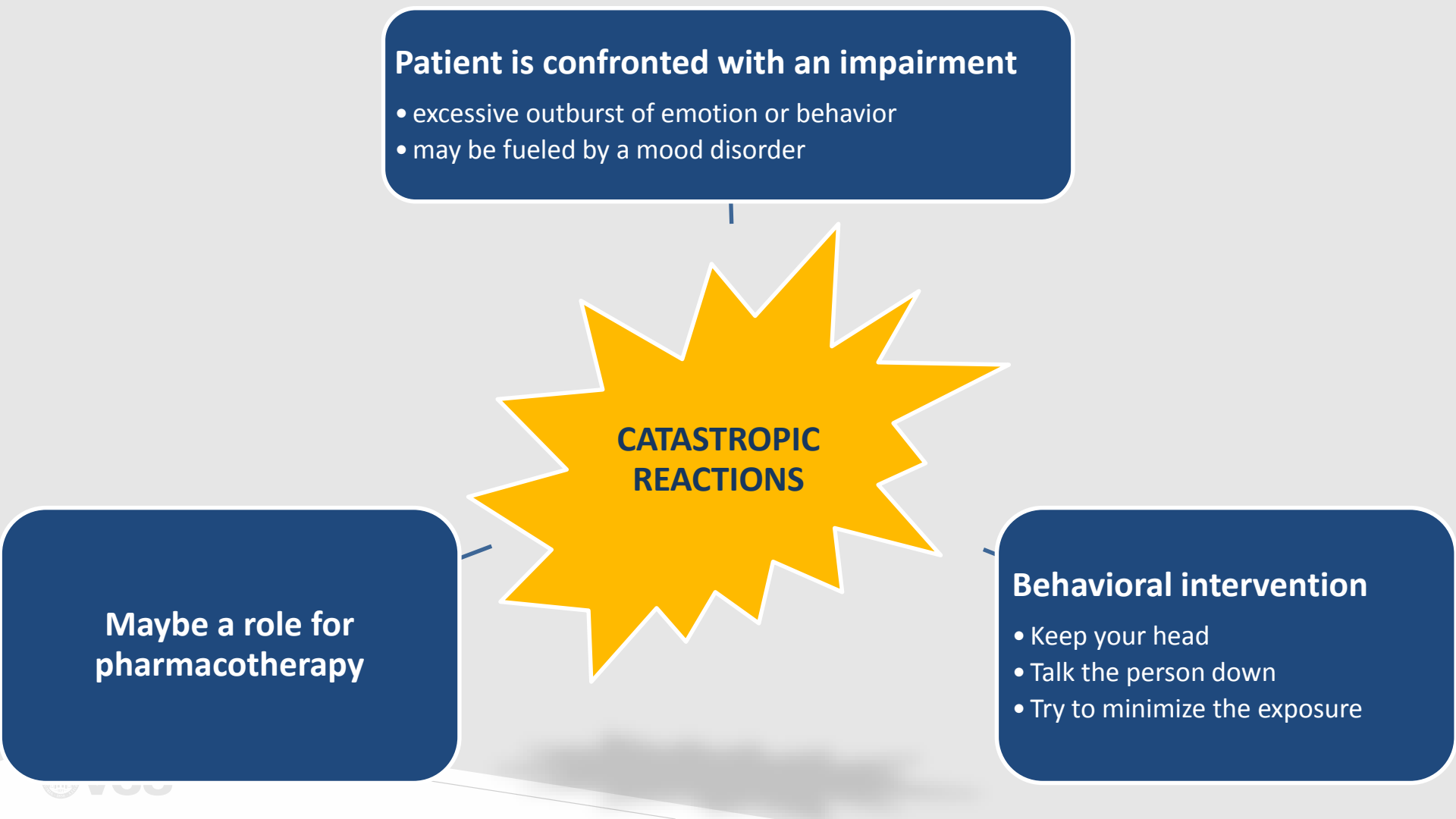
- Delusions: fixed, false, idiosyncratic beliefs
  - persecutory, mood congruent
  - may drive behavior
- Hallucinations: perceptions without stimuli
  - may be auditory or visual, or other
  - may be associated with visual impairment
- Psychosis doesn’t always require or respond to treatment
  - delusions confused with misinterpretation
  - hallucinations confused with confabulation

DELIRIUM

- Impaired ability to pay attention
  - waxing and waning consciousness
  - multiple psych symptoms may result
  - physicians are fooled by quiet delirium
- Look for a relatively sudden change in mental status
  - don’t ascribe it to a chronic condition
- Treatment is removal of the cause
  - polypharmacy
  - UTI
  - pneumonia/hypoxia

SLEEP DISTURBANCE

- Insomnia most common
  - can have complete reversal of the cycle
- Daytime sleepiness is also an issue
- Treat causative factors, e.g. depression
- Improve sleep hygiene
  - keep patient busy all day
- Sedatives should be the last, not the first resort


Patient is confronted with an impairment
• excessive outburst of emotion or behavior
• may be fueled by a mood disorder
CATASTROPIC REACTIONS
Maybe a role for pharmacotherapy
Behavioral intervention
• Keep your head
• Talk the person down
• Try to minimize the exposure

EXECUTIVE DYSFUNCTION SYNDROME

"Frontal" is a pseudoanatomical term

Hallmark is juxtaposition of apathy and disinhibition

Found in a variety of other dementias

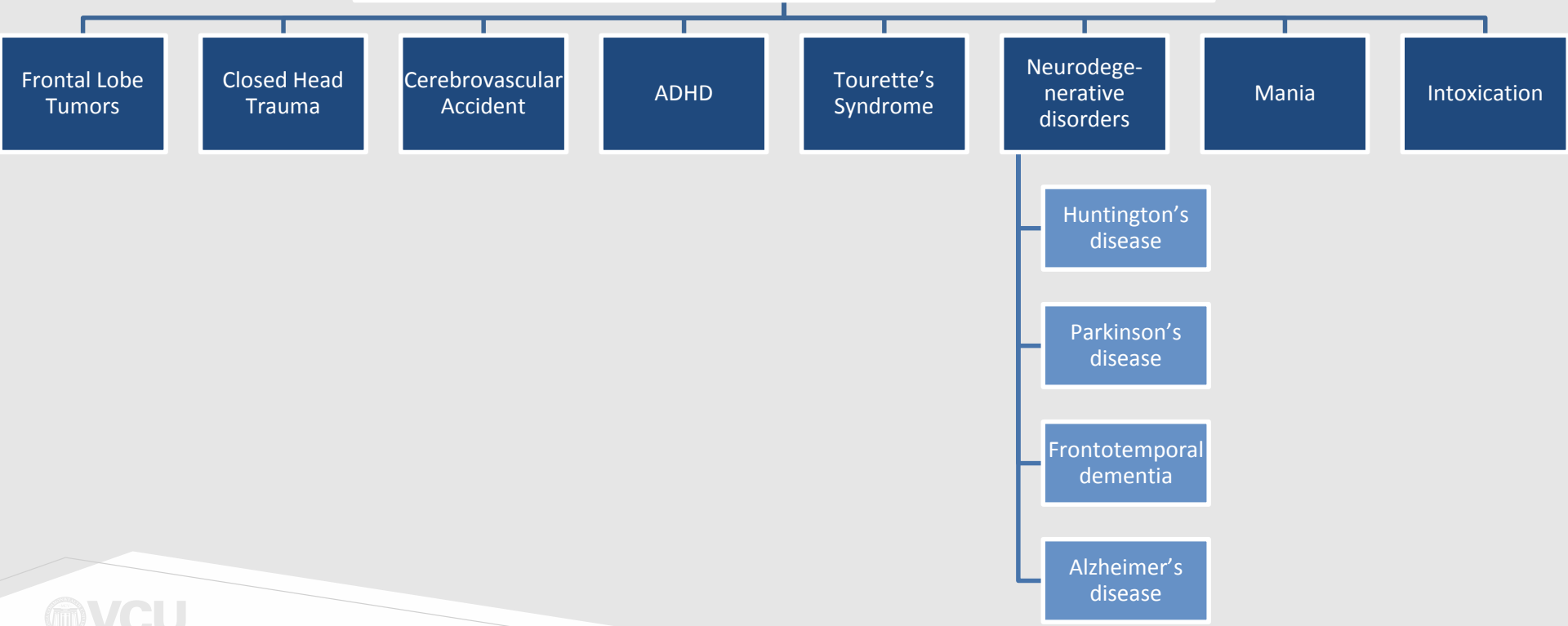
Particularly in subcortical conditions, e.g. Huntington disease, Parkinson's disease

Likely reflects dysfunction in multiple circuits connecting frontal lobes with subcortical matter.

Often a profound loss of insight

May be out of proportion to cognitive impairment

CONDITIONS ASSOCIATED WITH DISINHIBITION



Poll

Keeping patients on dementia drugs such as Aricept and Namenda is no longer necessary when they are in the advanced stages of dementia.

- ❑ True
- ❑ False

Use agents for dementia

Although agents specifically for dementia **do not modify the course of the disease**, research does support their effects on dementia related behaviors such as delusions/hallucinations, apathy, and agitation

Generally it is recommended to keep patients on these agents even at later stages of dementia

ANTIPSYCHOTIC MEDICATIONS FOR BEHAVIORAL PROBLEMS

Mixed results in studies but show some efficacy

Drugs include:

- quetiapine (Seroquel)
- risperidone (Risperdal)
- olanzapine (Zyprexa)
- haloperidol (Haldol) and others

Risks and side effects: dizziness, falls, sedation, cardiac problems

Poll

When a number of studies were analyzed, it was found that antipsychotics increased rates of death in dementia patients by about how much?

- ❑ 10x
- ❑ 2x
- ❑ 5x
- ❑ 100x

ANTIPSYCHOTIC BLACK BOX WARNING

In an analysis of 17 placebo controlled studies, the rate of death in the drug treated patients was approximately 1.7 times the rate seen in placebo treated patients

Over the course of a typical 10 week trial, the rate of death increased from about 2.6% to 4.5%

Most of the deaths appeared to be either cardiovascular or infectious (eg. pneumonia)

Schneider et al. JAMA. 2005 Oct 19;294(15):1934-43.

Are there MOOD STABILIZERS?

- Agents which treat mania or depression
- Agents which prevent affective episodes
- Agents which decrease emotional lability in patients with personality disorders
- Agents which treat disinhibition or agitation in demented patients

The existence of the term produces spillover

Mostly in reference to anticonvulsants

MOOD STABILIZERS

Very little research evidence but may still be seen in practice

Most common in dementia is divalproex (Depakote)

Risks and side effects: sedation, liver damage

POLL

Antidepressants are only used to treat depression in patients with dementia

- ❑ True
- ❑ False

ANTIDEPRESSANTS

Advantages in safety and tolerability	Sertaline (Zoloft), citalopram (Celexa), escitalopram (Lexapro) probably safest and easiest Mirtazapine (Remeron) also used
Could be used to target specific symptoms	Dysphoria, perseveration, apathy
Studies show benefit in non-depression-related “agitation” in dementia patients.	

ANTIDEPRESSANTS

Risks and side effects:

- Sedation
- Dizziness
- Falls
- Low sodium
- Cardiac problems

ANTIDEPRESSANT CASE EXAMPLE

82-year old married woman

Mild dementia, insidious onset and gradual progression.

Diagnosed with Alzheimer's disease.

She is convinced that her husband is having an affair.

She can no longer recognize her own clothes and claims they belong to his "sloozy" (a neologism).

She interprets wrong numbers as being calls from his girlfriend.

She admits she has never seen her, but claims he sneaks her in and out.

Her husband is 90 years old and blind.

She has taken to writing hostile messages for this woman on the mirrors in their home.

Marital relationship is becoming increasingly strained.

She cannot go more than a few minutes without bringing up the subject in the doctor's office.

She has already been treated with three different neuroleptics, with no benefit, and is taking donepezil.

On the latter medication, her MMSE has risen 2 points, but the obsessive jealousy persists.

She is started on 25mg of sertraline, advancing to 50mg after 1 week.

She stops writing on the mirrors and her relationship with her husband improves markedly.

On a follow-up visit she is asked about his fidelity. She replies that she knows he is still being unfaithful, but no longer feels the need to argue about it.

She is comfortable in her longstanding marriage and rarely thinks about the affair

Amphetamines (stimulants)

- Could target specific “frontal” symptoms
  - Apathy
  - Distractibility
  - Disinhibition
- Physicians fear to make an disinhibited patient worse
  - Yet stimulants help to focus attention in ADD
- Some promising results in studies
- Caffeine has also been studied for apathy
- Risks and side effects: appetite suppression, cardiac problems

AMPHETAMINE CASE EXAMPLE

79-year old woman brought in by her daughter

Moderately severe dementia

She is dressed in her daily outfit of a conservative suit and wears a large crucifix.

She still attends church every day, but otherwise spends most of the time sitting silently, or telling the rosary over and over.

She seldom speaks, even in response to questions.

She refuses most food and has been observed emptying plates or cups into potted plants when she thinks no one is looking.

She has lost a great deal of weight.

Her apathetic presentation is punctuated by sudden bursts of odd behavior.

She is mostly silent during the interview, but at one point gets up, crosses the room to hug and kiss the examiner, and then lies down on the floor of the office, refusing to get up until the interview is over.

She is given a diagnosis of a non-Alzheimer's dementia.

She has not respond previously to neuroleptics, which were tried on the assumption that she was suspicious about the food.

She also did not respond to an antidepressant, started on presumption of depression.

Targeting her apathy, she is treated with 5mg a day of dextroamphetamine, with an increase to 5mg bid.

Within a few days of starting the stimulant she has begun to eat again and to communicate better.

At a follow-up visit a month later, she is verbal and scores a 21 on the MMSE.

She has gained some weight and there are no odd behaviors.

AMANTADINE

Was regarded as bottom of the barrel for “agitation”

Precise mechanism is unknown

Believed to be related to dopamine augmentation

Used with patients at JHH

Drayton et al. Psychosomatics 2004; 45:205–209

Behavioral Management of Disinhibition

Reduce the opportunities for disinhibited behavior

- Manage the environment
- Avoid surprises and broken promises

Establish a regimen of positive activities

- Maintain a regular schedule
- Allow rest but avoid extensive downtime

Do not adopt a punitive approach

- Disinhibited patients are relatively insensitive to punishments and reward alike
- Need to avoid conflict altogether

AMANTADINE CASE EXAMPLE

63-year old man admitted to hospital.

Has rapidly progressive dementia of recent origin.

18 months ago he was running an auto repair shop.

For long periods of the day he will sit quietly and interact congenially when spoken to.

Served in the navy as a younger man and often believes he is at sea.

At other times he will become restless and anxious, intrude into other patients rooms, try to leave the units, will have striking visual hallucinations, and engage in bizarre behavior.

In one instance he discovered a janitor's bucket, and dumped several gallons of water on the floor of the nurses' station, shouting, "The ship is on fire!"

After an extensive workup he is given a diagnosis of frontotemporal dementia.

His behaviors do not respond to redirection, and treatment trials of typical and atypical neuroleptics, an SSRI, and divalproex sodium are unsuccessful.

Neuroleptics seem, if anything, to exacerbate his behavior.

His need for 24 hour a day supervision is placing a strain on the unit. One morning he grabs his psychiatrist by the lapels and says "Doc you've got to help me!"

He is started on amantadine 50mg bid, which is advanced to 100mg bid and within a few days there is a complete resolution of all his behavioral symptoms.

He stops hallucinating and wandering.

His behavior is directable.

He engages in occupational therapy. Constant observation is discontinued. He is placed in a nursing home, where, within a few days he kicks out a section of a fence to escape.

He is readmitted to the hospital and his dose of amantadine is raised to 100mg tid.

He returns to the nursing home where he makes a satisfactory accommodation.

Six months later his problem behaviors have reemerged.

He returns to the hospital and his dose is raised to 200mg bid with good results

Other miscellaneous drugs

Trazodone	used for sleep and occasionally daytime agitation, some evidence to support use for sleep
Benzodiazepines	used for sleep and daytime agitation, minimal evidence to support
Zolpidem (Ambien)	no evidence in dementia but appears to be relatively safe in elderly at low doses
Pregabalin (Lyrica) or gabapentin (Neurontin)	may be used for anxiety/sleep, some evidence

New drug approaches

Dextromethorphan-quinidine (Nuedexta)

- currently approved for PBA

Brexpiprazole (Rexulti)

- currently approved for treatment of MDD

Prazosin (Minipres)

- currently used for PTSD

Cannabinoids

- being studied

Pimavanserin (Nuplazid)

- currently approved for psychosis in Parkinson’s

Several other new agents under investigation

Poll

Medications should be the first intervention to use for challenging behaviors associated with dementia.

- ❑ True
- ❑ False

Remember…

Behavioral problems in dementia are the most treatable aspects of the disease

To choose the right tool, you have to know what the job is

Not every psychiatric disorder is in the DSM

Not all unusual behaviors in dementia require pharmacologic, or any, treatment.

NON-INTERVENTION CASE EXAMPLE

45 year old man with Huntington's disease

Brought to the clinic by his brother for concerns of "depression".

The brother reports that he spends all day sitting on the couch watching television.

He eats and sleeps normally and attends to his hygiene with reminders.

Recently, it was the patient's birthday and his brother arranged for the two of them to go fishing, an activity the patient previously enjoyed.

The patient was reluctant to leave the house, but once outdoors behaved more or less normally while fishing and actually caught several fish.

When they retuned home, he resumed his seat in front of the television, did not say thank you, and would not discuss the fishing trip further.

On examination he is casually dressed and not malodorous.

He has intermittent chorea in all four extremities.

Speech is mildly dysarthric.

He describes his mood as "good" and denies change in self-attitude or vital sense, pessimism, or suicidality.

When asked if he is able to enjoy things he replies that he enjoys television.

He is puzzled by his family's attempts to get him out of the house.

There are no delusions or hallucinations.

He scores 24 out of 30 on the MMSE

It is explained to the brother that this apathy and constriction of activities is a common symptom of Huntington's disease, that the patient is not depressed and does not appear to be suffering.

He is told that his brother will have more trouble initiating rather than sustaining behaviors, as on the fishing trip.

The brother feels reassured and adjusts his expectations.

On the patient's next birthday, he and his brother watch a football game together on television.

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