PHARMACOLOGIC MANAGEMENT OF BEHAVIORAL AND NEUROPSYCHIATRIC SYMPTOMS OF DEMENTIA

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NEUROPSYCHIATRIC SYMPTOMS IN DEMENTIA

Behavioral and psychological symptoms of dementia occur commonly in dementia. While they are not a core symptoms of dementia, they occur in almost every patient with dementia. These symptoms can be divided into roughly 12 categories.

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Description (from NPI-Q)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Delusions</td>
<td>Does the patient have false beliefs, such as thinking that others are stealing from him/her or planning to harm him/her in some way?</td>
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<tr>
<td>2. Hallucinations</td>
<td>Does the patient have hallucinations such as false visions or voices? Does he or she seem to hear or see things that are not present?</td>
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<tr>
<td>3. Agitation/Aggression</td>
<td>Is the patient resistant to help from others at times, or hard to handle?</td>
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<tr>
<td>4. Dysphoria/depression</td>
<td>Does the patient seem sad or say that he/she is depressed?</td>
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<tr>
<td>5. Anxiety</td>
<td>Does the patient become upset when separated from you? Does he/she have any other signs of nervousness such as shortness of breath, sighing, being unable to relax, or feeling excessively tense?</td>
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<tr>
<td>6. Euphoria</td>
<td>Does the patient appear to feel too good or act excessively happy?</td>
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<td>7. Apathy</td>
<td>Does the patient seem less interested in his/her usual activities or in the activities and plans of others?</td>
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<tr>
<td>8. Disinhibition</td>
<td>Does the patient seem to act impulsively, for example, talking to strangers as if he/she knows them, or saying things that may hurt people's feelings?</td>
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<tr>
<td>9. Irritability/Lability</td>
<td>Is the patient impatient and cranky? Does he/she have difficulty coping with delays or waiting for planned activities?</td>
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<tr>
<td>10. Motor Disturbance</td>
<td>Does the patient engage in repetitive activities such as pacing around the house, handling buttons, wrapping string, or doing other things repeatedly?</td>
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<tr>
<td>11. Sleep Disturbance</td>
<td>Does the patient awaken you during the night, rise too early in the morning, or take excessive naps during the day?</td>
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<tr>
<td>12. Appetite Changes</td>
<td>Has the patient lost or gained weight, or had a change in the type of food he/she likes?</td>
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FREQUENCY OF NEUROPSYCHIATRIC SYMPTOMS IN DEMENTIA

About 97% of individuals with dementia are affected.

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<tr>
<td>Apathy 49%</td>
<td>Appetite 34%</td>
</tr>
<tr>
<td>Depression 42%</td>
<td>Motor disturbance 34%</td>
</tr>
<tr>
<td>Aggression 40%</td>
<td>Delusions 31%</td>
</tr>
<tr>
<td>Anxiety 39%</td>
<td>Disinhibition 17%</td>
</tr>
<tr>
<td>Sleep disturbance 39%</td>
<td>Hallucinations 16%</td>
</tr>
<tr>
<td>Irritability 36%</td>
<td>Euphoria 7%</td>
</tr>
</tbody>
</table>

(Zhao JAD 2016)
Neuropsychiatric Symptoms

Often begin early in the course of dementia yet are often under-recognized. Sometimes they occur in advance of dementia and are an early indication that something has changed with the individual. They tend to be persistent in the course of the illness, but can vary in severity and presentation over time. Their variation is not trait dependent, but rather state dependent.

(Steinberg M 2004, Vik-Mo AO 2017).

Different symptoms may be more frequent, depending on the type of dementia (i.e. increased apathy in Alzheimer’s disease, increased hallucinations in Lewy Body Dementia, increased disruptive behaviors in behavioral variant Frontotemporal Dementia).

What Impact Do These Symptoms Have on the Individual with Dementia?

These symptoms have significant impact on the affected person, including:
- Interference in activities of daily living
- Lower quality of life
- Faster disease progression
- Higher cost of care
- Earlier institutionalization

(Gonzalez-Salvador T 2000, Peters ME 2015, Lanctot KL 2017)

What Impact Do These Symptoms Have on the Caregiver?

Neuropsychiatric symptoms have a significant effect on caregivers. Neuropsychiatric symptoms are predictive of caregiver burden and depression, regardless of dementia diagnosis. The effects appear to be driven primarily by disruptive behaviors:
- Agitation
- Aggression
- Disinhibition
- Delusions
- Mood disturbance

Secondarily by:

Disruptive behaviors affect the emotional connection between the caregiver and the person with dementia. They also make it hard to provide care for activities of daily living, like bathing, dressing. These behaviors can occur with any type of dementia, but can be more frequent in certain types of dementia, such as Frontotemporal Dementia. NPS are generally more disturbing to caregivers in comparison to a loved one’s memory loss or functional impairment.

Neurobiology of BPSD in Alzheimer’s Disease

There is a limited understanding about how the neuropathological changes in Alzheimer’s Disease correlate with these associated behavioral and psychological symptoms.

While the type of symptom may indicate a likely region of brain involvement (e.g. the hypothalamus and appetite or sleep), this exact relationship has yet to be fully elucidated. A focus on subcortical structures is needed.

Understanding the neurobiology of NPS may help us develop better treatments.
FIRST STEPS IN TREATMENT

1. Address all medical issues, including untreated pain (PAIN-AD scale can help determine unreported pain)
2. Get rid of medications that might be contributing to the problem (i.e. high anticholinergic medications)

FOCUS ON CAREGIVERS

Nonpharmacologic interventions delivered by caregivers can reduce the frequency and severity of neuropsychiatric symptoms.

These interventions include skills training, education, communication training, problem solving, and ongoing support. The most successful interventions included 9-12 sessions delivered in the home and tailored to the needs of the person and their caregiver, with periodic follow up. Effect sizes of 0.34 were demonstrated.

(Brodaty H Am J Psych 2012)

EFFICACY OF SPECIFIC INTERVENTIONS

Interventions studied:

- Aromatherapy, massage, acupressure, cognitive stimulation, reminiscence therapy, simulated presence therapy, animal assisted therapy, cognitive/emotion oriented therapy, dance therapy, music therapy, and in-home or facility-based behavioral management.

- Only Music therapy and behavioral management techniques have demonstrated reductions in neuropsychiatric symptoms of dementia.

(Abraha I, BMJ 2017)

NEUROPSYCHIATRIC INVENTORY QUESTIONNAIRE (NPI-Q)


www.NPItest.net

MEDICATION TREATMENT

ANTIDEPRESSANTS
### ANTIDEPRESSANTS

1. Selective Serotonin Reuptake inhibitors may provide relief in depression, agitation, and anxiety. (Seitz DP 2013, Leonpacher AK 2016, Viscogliosi G 2017)
2. Those with moderate agitation and with lower levels of cognitive impairment were more likely to benefit from citalopram, and those with more severe agitation and greater cognitive impairment were at greater risk for adverse responses.

### ANTIPSYCHOTICS

#### SECOND GENERATION ANTIPSYCHOTICS (SGA)

In 2010, SGAs were prescribed in up to 60% of patients with dementia who were in facilities. (Gentile S 2010). Slight decrease after FDA warning about in increase mortality. But sometimes a necessary choice for significant aggression. Ironically, may not work all that well for psychosis.

#### IF YOU PRESCRIBE:

1. START at a low dose: risperidone 0.25 mg, olanzapine 2.5 mg, aripiprazole 2.5 mg
2. Terminal doses: risperidone 1 mg bid, olanzapine 10 mg qhs, quetiapine 100 mg bid
3. Only use SGA, don't use first generation antipsychotics (i.e. Haldol), higher risk of side effects including stroke (Hsu W 2017)
4. Monitor for side effects
IF YOU PRESCRIBE:
1. Monitor for potential benefit. Presence/absence of response at week 2, was associated with response or non-response at week 8 (Yoshida K 2017).
2. Don’t use higher EPS antipsychotics (i.e. risperidone, abilify) in LBD or Parkinson’s dementia.

SGA: TO CONTINUE OR NOT
Convention has always been to make regular attempts to withdraw antipsychotics because of risks associated.

Recent Cochrane analysis (Van Leeuwen E 2018) found that for patients with less severe NPS at baseline, it may be prudent to discontinue antipsychotics. For patients with more severe aggression, agitation, or psychosis, symptom relapse was likely, therefore this subgroup may need to STAY on antipsychotics if they have been effective.

OTHER MEDICATIONS THAT MIGHT WORK
1. MEMANTINE:
Recent Meta analysis (Kishi T 2017) showed that compared to placebo, memantine showed significant benefit in agitation, aggression, delusional thinking, disinhibition, and sleep disturbance.

2. ANTICHOLINESTERASE INHIBITORS:
Mixed results but may have some benefit (Masopust 2018, Campbell 2008). Watch for Side effects: diarrhea, nausea, bradycardia, syncope.

3. MOOD STABILIZERS:
Only carbamazepine has shown to work, and for aggression. Valproate does NOT work. (Yeh Y 2012). Oxcarbazepine and lithium had low efficacy.

4. PRAZOSIN:
One tiny RCT (n=22) showed that subjects taking a mean dose of 5.7 mg had significant improvement in agitation and aggression compared to placebo. Watch for dizziness and hypotension.

5. Mirtazapine:
One small open label study. Might work for agitation, sleep disturbance. Not enough data yet.

6. TRAZODONE:
Was helpful for NPS in Frontotemporal dementia (Lebert F 2004)

7. BENZODIAZEPINES:

8. MELATONIN:
No demonstrated benefit. (Gehrman PR 2009)
CONCLUSION

- Neuropsychiatric symptoms occur in 97% of patients with dementia and they tend to be chronic.
- Always ask about them. Better yet, use the Neuropsychiatric Inventory Questionnaire to screen for them.
- These symptoms have a significant effect on the person experiencing them AND the caregiver.
- Behavioral management is critical
- Medication management can be helpful. Start with antidepressants.