



Pharmacological Treatments

Declaration of real or potential conflicts of interest

Name of speaker: René Desautels, MD, FRCP, Medical Chief of the Moe Levin Unit



Over the last 2 years I have had or have presently an affiliation, financial interest or others with a commercial enterprise or I have received wages, flat rate or research grants from a commercial enterprise in relation with the contents of this presentation.

Name of the enterprises	Type of affiliation	Date
MERCK	Clinical Research	2017
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BIOGEN	Clinical Research	2017
SUNOVION	Speaker	2017 – 02
OTHERS	Clinical Research	2018-2019

Declaration of real of potential conflicts of interest

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- I have no real or potential conflict of interest in regards to the contents of this presentation.**
- Off-label use of medications will be discussed in this presentation.**

NPS

(Neuropsychiatric Symptoms)

The importance of the algorithm in the evaluation of NPS: The right patient, at the right time, in the right place!

Evaluation of the NPS

- To description
- To quantify it (NPI, Cohens Mansfield)
- To target: observation grid for the more complex cases

List of the NPS most frequently observed

The examination of patients with AD or another NCD should understand the tracking of the BPSD and other neuropsychiatric symptoms associated to these illnesses

The most premature NPS during AD

Apathy/Indifference*

Loss of decrease of motivation relating to behaviour, thoughts and emotions.

Depression*

Sadness, tearfulness, despair, feeling of helplessness, low self esteem, guilt

Anxiety*

Feeling of an imminent and undetermined danger
Internal state characterized by:

- Thoughts (apprehension, diverse causes of concern).
- Emotions (anxiety and fear).
- Physical sensations (muscular tensions, shortness of breath, gastro-intestinal malaise, headaches).
- Behaviour (avoidance, repetitive requests, excessive dependence, agitation).

Irritability*

Mood instability, low tolerance level

Aggressivity/Agitation*

Verbal agitation (screaming, yelling, constantly talking) and physical (throwing objects, spitting, pinching, scratching) with or without aggressivity.

Classification of the NPS

Affective and Emotional Disorder*

- Depression
- Anxiety
- Irritability
- Emotional lability
- Mood exaltation (euphoria).

Behavioural Disorders*

- Wandering
- Repetitive vocalization
- Repetitive movements or stereotyped
- Aggressive disinhibition
- Sexual disinhibition
- Usage behaviour
- Imitation behaviour

Psychotic Disorders*

- Hallucinations
- Delusions
- Identification Disorder

Neurodegenerative Disorder*

- Sleep (wandering at night, Sundowning, Wake-Sleep cycle reversal)
- Eating and orality Disorder

*12 behaviour problems referenced with the help of the shorten version of the neuropsychiatric inventory (NPI-RI)

**The importance of the algorithm in the evaluation of NPS:
The right patient, at the right time, in the right place! *(continued)***

Nurse

- Evaluation of the approach
- Clinical Evaluation
- Evaluation of the needs
- Psychosocial Evaluation
- Evaluation of the environment

Doctor

- D_x NPS
- Unstable medical condition of delirium
- Decompensated Mental Health
- Medication
- Evaluation of the dangerousness

A – Pre-Dx

- 5 years prior
- Most w/i 2 years prior
- ▲ Personality, disinhibition
- Lack empathy, ▲ attitude towards family (will, etc...)
- Gambling, fights, sexual
- ▲ Judgement and values
- Affective ▲ 's
- Delusions
- Hallucinations

B - Epidemiology

- 97% will show NPS
- MCI patients also ($\pm 60\%$)
- Median duration 18 months
- 6 months – 3 years
- Symptoms fluctuate
- Recurrence of 30-50%

C - Epidemiology

- ↑ severity NPS → ↑ dementia progression
- Meta-analyses (Zhao, Tan et al. 2016)
- 48 articles
- Apathy 48%
- Depression 42%
- Aggression 40%
- Anxiety 39%
- Sleep Disorders 39%

D - Epidemiology

- Mild behavioral Impairment checklist (MBI-C)
- 16 items (max 48)
- On autopsy; ↑ p-TAU correlates with agitation
- TBI correlates with agitation

E – NPS and Medications

- Aggression
- Agitation
- Psychosis
- Depression
- Anxiety
- Apathy
- Sleep

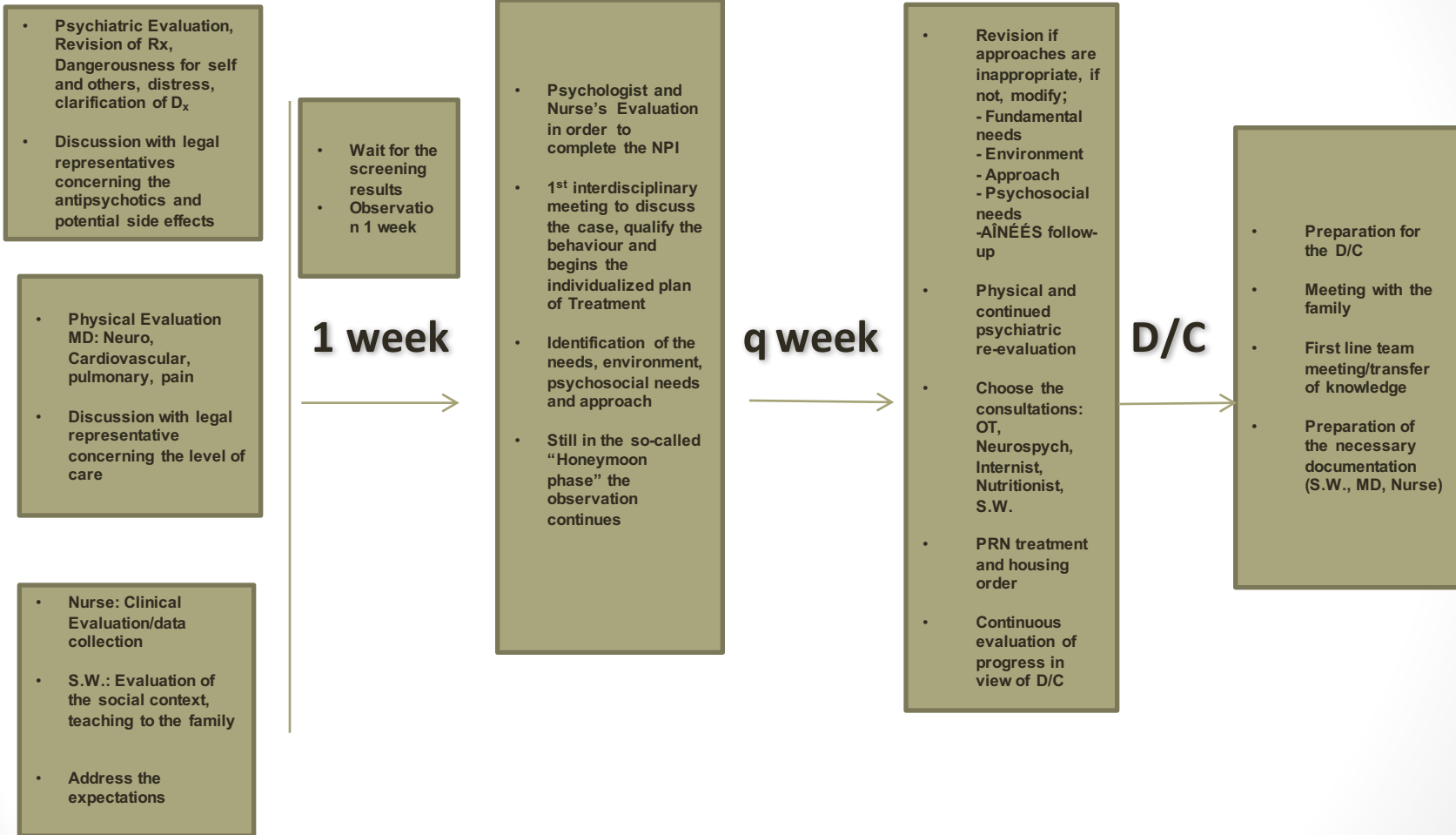


**KEEP
CALM
AND
DON'T
PANIC**

© 2009

Journey of a hospitalisation at the MLU 3rd line (1st in Qc)

Admission



Objective of the treatment

Regulate Arcadian rhythm

Think about akathisia

- ↓ Anxiety ↓ depression ↓ fear ↓ distress ↓ agitation
- ↓ Neuropsychiatric symptoms while avoiding side effects
- ↓ The intensity and frequency of hallucinations and deliriums
- ↓ ‘Cocktail’ Approach and ↓ dose for ↑ effect
- ↓ Anxiety ↓ depression ↓ fear ↓ distress ↓ agitation
- ↓ The intensity and frequency of hallucinations and deliriums

GOALS

- ↓ Danger for self and others
- ↑ Cognitive functions with improvement of the affect
- ↑ Return to residences/IR/CHSLD/Hospital

Limitations of pharmacological treatments

Refusal of Tx by the person

- Necessity to procure a court order IM/PO/PRN (risk in terms of time)

Atypical antipsychotics

- Quetiapine, Risperidone, Olanzapine, Clozaril

Intra muscular

- Loxapac +/- Ativan
- Clopixol accuphase: limited choice in regards to the clientele's fragility (EPS)
- Clopixol Depot
- ❖ **New atypical antipsychotics = risk is always high for EPS** (*Extra Pyramidal Symptoms*)
- Other treatment: ECT (obtaining consent)

Potential side effects

- EPS
- ↓ mobility
- Dysautonomia (B.P., orthostatic hypotension, hypoperfusion)
- ↓ left ventricular ejection fraction; ↑ Qtc; ↓ Na⁺
- Sedation, confusion, delirium (direct/indirect effect)
- ↑ risk of death (falls, strokes...)

Attention!

Pet peeves

- Anti cholinergic
- Anti histaminic
- Benzodiazepine
- Atypical antipsychotics

Lewy Body Dementia/PSP/Parkinsons

Sensitive Atypical antipsychotic; side effects;

- Dysautonomia, constipation, EPS, pneumonia

Proposed treatments:

- Gabapentin, Trazodone
- Oxcarbazepine, Phenytoin
- Quetiapine, Clonazepam
- ECT + Tdc's
- Pimavanserin (non dopaminergic, potentially weak A.A. dopamimergic) ↓ visual hallucination/delirium without ↑ Parkinsons
- Armodafinil ↓ apathy ↓ visual hallucinations ↓ agitation

Head trauma, CVA, hypoperfusion

- AD-5HT
- Trazodone; no benzo
- Gabapentin
- Phenytoin, Valproate, Levetiracetam
- Bupropion
- Propranolol
- Guanfacine (less sedative and hypotensive than Clonidine)
- Stimulants

NPS Treatments

Choreiform Movements (Huntington's Disease)

- ↓ Dopamine, Catecholamine
- Nitomane (late dyskinesia)

Hypersexuality

- Standard Tx: Androcur; ↓ synthesis testosterone

Lack of empathy (FTD)

- Intranasal Oxytocin
- Serotonergic Antidepressor

Emotional Apathy/Lability

Apathy

- Bupropion, Vortioxetine
- Methylphenidate and others
- Modafinil, armodafinil
- rTMS, tDCs

Emotional Lability

- Dextromethorphan, Quinidine (20 – 10 mg)
- Carbamazepine, Valproate, Gabapentin
- Cholinesterase Inhibitor (little effect on the delay of the apparition of it)

Considering new treatment paradigms for neuropsychiatric symptoms of Alzheimer's disease

Krista L. Lancôt, Brendon P. Boot, Lisa J. Bain, James A. Hendrix, Marcia C. Carrillo

Abstract 7

DOI: <http://dx.doi.org/10.1016/j.jalz.2016.09.002> | CrossMark

Abstract Full Text References

Neuropsychiatric symptoms (NPS) – especially apathy, depression, agitation, psychosis, and sleep disorders – are among the most prominent and distressing symptoms of people with Alzheimer's disease (AD), yet they remain under-recognized, and effective treatments are limited. The Alzheimer's Association's Research Roundtable (AARR), a consortium of scientists from academia, industry, and regulatory agencies, explored the nature, complexities, and possible avenues for improved treatment at its spring meeting May 23-24, 2016, in Washington, DC.

Lancôt and Boot are co-first authors.

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January 2017 Volume 13, Issue 1, Pages S4-100

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Apathy associated with neurocognitive disorders: Recent progress and future directions

Krista L. Lancôt, Luis Agüero-Ortiz, Henry Brodaty, Paul T. Francis, Yonas F. Geda, Zahinoor Ismail, Gad A. Marshall, Moyra E. Morby, Chiadi U. Olyyike, Prasad R. Padala, Antonios M. Politis, Paul B. Rosenberg, Emma Siegel, David L. Sultzer, Eleanor F. Abraham

Abstract

Can J Psychiatry. 2017 Mar;62(3):158-160. doi: 10.1177/0706743716672409

Detecting and Managing Neuropsychiatric Symptoms in Dementia.

Iaboni A^{1,2}, Rapoport M^{1,2}

Author information

Curr Psychiatry Rep. 2016 Nov;18(11):103.

Apathy in Dementia: Systematic Review of Recent Evidence on Pharmacological Treatments.

Harrison F^{1,2}, Aerts L¹, Brodaty H^{3,4,5}

Author information

Abstract

Increasing recognition that apathy is one of the most prevalent behavioral and psychological symptoms of dementia and causes substantial caregiver distress has led to trials evaluating psychosocial and pharmacological treatments of apathy in dementia. We evaluated evidence of the efficacy of pharmacotherapies for apathy in dementia from studies since 2013. Previously reported benefits of acetylcholinesterase inhibitors and memantine were not replicated in recent studies. Antidepressants had mixed results with positive effects for apathy shown only for agomelatine, while stimulants, analgesics, and oxytocin study results were inconclusive. For some approaches, such as antipsychotic review, positive effects were found only in combination with nonpharmacological approaches. Relatively few studies assessed apathy outcomes specifically, complicating interpretation of potentially positive treatment effects; none dissected outcomes for emotional, motivational and behavioral components of apathy. Better trial design and more detailed analysis are needed in order to evaluate outcomes of pharmacological treatments for apathy.

Previous Article | CrossMark | Next Article

April 16, 2016
Platform Session
Aging and Dementia: Therapeutics and Management

Impact of Armodafinil Therapy on Neuropsychiatric Features in Dementia with Lewy Bodies (S1.004)

Karen Kuntz¹, Sara Mason¹, Maria Lapid², Jeremiah Aakre², Emily Lundt³ and Bradley Boeve¹

SHOW AFFILIATIONS
Neurology April 5, 2016 vol. 86 no. 16 Supplement S1.004

Abstract

ABSTRACT

Objective: Assess the effect of armodafinil therapy on neuropsychiatric features associated with dementia with Lewy bodies (DLB). Background: Common features of DLB are excessive daytime somnolence and neuropsychiatric features of visual hallucinations, agitation, anarchy, delusions, depression, anhedonia and anxiety. While wake-promoting

Amygdala and Hypothalamus

Historical Overview

Gouveia & al, Neurosurgery 85: 11-30, Jan. 2019

- Amygdala is heavily connected to hypothalamus and prefrontal cortex.
- Very implicated in Impulsive aggressivity contrary to premeditated aggressivity.
- In Humans, Amygdala stimulation increases aggression.
- Medications:
 - Meds used for the primary psychiatric-neurological condition; typical and atypical antipsychotics; antidepressants, cognitive enhancers; anti epileptics, mood stabilizers (Lithium), stimulants, etc...

Amygdala and Hypothalamus *(continued)*

- First monotherapy, then polypharmacy.
- Electroshock Therapy.
- DBS (Deep-brain stimulation).
- Stereotoxic neurosurgery.
- Heterogeneity of patients and symptoms → no 'one size fits all'
- Anticonvulsants for behavioural and psychological symptoms in dementia: Protocol for a...(on-going)

Amygdala and Hypothalamus *(continued)*

- **Trazodone**
 - May help for insomnia, sundowning and daytime agitations (↑ sleep duration by 42.5 mins (*Cormagos, AM. J, Geri. Psych. 2014*))
 - PRN usage?
- 2 small RCTs
- Worsened NPI (↑ 5 pts)
- Same risks of falls and fractures as antipsychotics

Amygdala and Hypothalamus *(continued)*

- **Prozasin**
 - Small (22 pts) study showed improvement in NPI (5.7 mg/day) without significant adverse effect
 - In practice → nil
- **Anti-epileptic medications**
 - See protocol for systematic ... Benj...& al. 2019
 - Divalproex, Carbamazepine and Gabapentin
 - Lack of consistent efficacy
 - Ø Valproic Acid

Amygdala and Hypothalamus *(continued)*

- **rTMS**
 - Small negative trial
- **Dextrometorphan – Quinidine**
 - Being studied
- 1 DB-RCT was +

Amygdala and Hypothalamus *(continued)*

- Ringman & Schneider Treatment options for Agitation in Dementia, Neurol (2019) 21:30.
- 23% of hospitalizations of ≥ 70 years is for:
 - Celexa 30 mg (40% vs 26% NPI-A)
 - best for MMSE > 20

Amygdala and Hypothalamus *(continued)*

- AA (Risperidone, Aripiprazol in RDBPC)
 - Efficacy around 18% ↓
 - No AA is more effective
 - 2^o black box warnings, AA reserved for non-responders to other measures or medications. Different in Canada where Risperidone has official indication.
 - Pimavenserin for hallucinations and delusion in LBD or Parkinson's disease.
- In 3 trials, non effective
 - Rivastigmine and other Anticholinesterase Inhibitors have modest efficacy in improving both cognition and behaviour.

Amygdala and Hypothalamus *(continued)*

- Pimavenserin for hallucinations and delusion in LBD or Parkinson's disease.
- In 3 trials, non effective
 - Rivastigmine and other Anticholinesterase Inhibitors have modest efficacy in improving both cognition and behaviour.

THC has potential: *Rosenberg & al.: Jap 2019/5/014*

- 2 major cannabinoid receptors
CB1: anxiolytic and euphoric effects primary in CNS also adipore
CB2: possible anti-inflammatory effects – mostly found in cells of immune system
- 10 mg = 2 mg Nabilone

THC

- THC 7 mg case series 40 AD-Inpatients mild improvement of mean agitation score
- RTC of THC 4.5 mg QD x 3 weeks was negative

- Mermarin & al. Cur Opin Psychiatry 2018, 31:140-146: RTC – crossover trial (added to regular psychiatric medications) 39 AD out-patients and Nursing homes mildly agitated but severely demented 6-5 crossover study
Mean...age 87 y.o. results moderate effect size
- NIH – funded RTC of Dronalbinol – Results to come

Dextromethorphan/Bupropion: Stephen M. Stahl, CNS Spectrums (2019) 24, 461-466.

- Dextromethorphan: NMDA – antagonist with multi modal activity.
- Bupropion: AD with Cytochrome P450 2D6 Inhibitor,
- Inhibition of 2D6 increases levels of Dextramethorphan.
- Dextromethorphan profile of actions is similar to Ketamine
- Studies both in depression and NPS

Prazosin

- Antagonizes Norepinephrine effects at brain postsynaptic Alpha-1 adenoreceptors.
- Statistically and clinically significant differences favoring Prozasin over placebo.
- Small numbers and high-dropout rate.
- 22 Nursing homes study.
- 2 groups of 12 patients → 11 vs 11.
- Drop out rate of 46%.

Wang & al. Am. J. Geriatric Psychiatry: 2009-Sept 17 (9)

Dexamethorphan/Quinidine

- Randomized clinical trial, 10 weeks.
- Not double blind.
- Partly crossover.
- 198 pts finished study.
- D-Q group ↓ NPI at $p < .001$

Gabapetin & Pregabalin

- Review and case report.
- No DBRCT study.
- 15 articles in case series.
- 12/15 positive.

Supasitt Humrong & al. BrJ. Clin. Pharmacol. (2019) 85: 690-703.

ECT



- ECT-AD
- NIA-Funding multi-site, single blind ECT & usual care (UC) vs Sham-ECT + UC
- Refractory to meds
- Recruit 200 pts (to come)
- Preliminary open-label data is safe and effective in reducing agitation in refractory UC pts with AD

ECT



- Prospective 23 pts
- Used Cohen-Mansfield
- 18/23 were positive

ECT



- Retrospective chart review
- 16 pts
- Only 2 with transient post-ictal confusion requiring Tx
- Can be efficacious for “screamers”

How long treatment

- Open label Risperidone responders to placebo/continuation

• Discontinuation:	16 w.	32 w.
Relapse rate {		
-Risperidone	33	15%
-Placebo	60	48%

Devanand, New Eng. J. Med., 2012

Agents in Development

- 15 studies on going
- Deudextromethorphan/Quinidine
- Dextrometorphan/Quinidine-Bupropion
- Lumateperone
- Scyllo-inositol

Agents in Development

- Brexiprazole (1 + DB-RTC, 400 pts) and 1-DB-RTC negative other study started
- Pimavenserin

Agents in Development

- Lumateperon
AA potent antagonist 5-HT 2A recep + 5-HT recep Inh +
Presynaptic agonism and post-synaptic antagonism D₂ recep
+ high affinity binding a D₁ recep + ↑ glutamate + in TOR
pathway
- Cannabis oil (CBD₂)
- Dronabinol
- Intranasal Oxytocin
- Lithium
- Carbamazepine

Ahmed & al. Drug & Aging (2019) 36: 589-605

Pimavenserin



- FDA approved for LBD's psychosis.
- Phase II DB-RTC on = 181.
- NPI – psychosis 55% had 30% improvement and placebo had 37%.
- But no difference at 12 weeks.

Citalopram



- Many more studies
- 1 DB-RTC total n: 186 was positive for agitation
- However, ↓ cognition and ↑ Qtc

Escitalopram



- S-enantiomer
- 1 DB-RCT Escitalopram vs Risperidone
- Escitalopram = Risperidone for agitation and psychosis
- No placebo group
- 1 DB-RCT for AD-Depression was negative

Cannabinoids

- 1 DB-RCT ongoing
- 12 mg CBD + 0.6 THC

CANNABINOIDS
THE ULTIMATE GUIDE TO CANNABIS MEDICINE

	THC	CBD	CBG	CBN	CBC	THCV	CBGA	CGCA	CBCA	THCA
Relieves Pain	●	●		●	●		●			
Reduce Seizures		●				●				
Sleep Better				●						
Relieve Anxiety		●								
Reduce Blood Sugar		●								
Suppress Appetite			●							
Kill/Grow Bacteria		●	●							
Reduce Nausea	●	●								
Anti-Fungal									●	
Inhibit tumor/cancer		●	●		●					●
Reduce Artery Blockage		●								
Treat Psoriasis		●								
Antipsychotic		●								
Suppress Muscle Spasm	●	●						●		●
Stimulate Appetite	●									
Promote Bone Growth		●	●		●	●	●			
Reduces Inflammation		●	●		●		●	●		●

CANNABINOIDS
THE ULTIMATE GUIDE TO CANNABIS MEDICINE

	THC	CBD	CBG	CBN	CBC	THCV	CBGA	CGCA	CBCA	THCA
Relieves Pain	●	●		●	●		●			
Reduce Seizures		●				●				
Sleep Better				●						
Relieve Anxiety		●								
Reduce Blood Sugar		●								
Suppress Appetite			●							
Kill/Grow Bacteria		●	●							
Reduce Nausea	●	●								
Anti-Fungal									●	
Inhibit tumor/cancer		●	●		●					●
Reduce Artery Blockage		●								
Treat Psoriasis		●								
Antipsychotic		●								
Suppress Muscle Spasm	●	●						●		●
Stimulate Appetite	●									
Promote Bone Growth		●	●		●	●	●			
Reduces Inflammation		●	●		●		●	●		●

Leafly

Dronabinol



- THC – analog full CB, and CB₂ agonist had crossover DB-RCT. Promising results but cross-over carry-over effects.

Nabilon



- Partial CB₁, and CB₂ agonist
- 1 DB-RCT m=39
- Overall NPI-scores improvement
- ↓ NPI – agitation/aggression
- Possible tolerance and ↑ confusion

Deudextromethorphan



- Deuterium atoms ↓ catabolism
- Still with Quinidine but less needed
- Hope is less cardiac SE than Quinidine
- Phase II placebo controlled multi-center.

Scyllo-Inositol



- Endogenous Inositol stereoisomer
- Hypotized to bind and inhibits AB42 aggregation
- 2 negative DB-RCT

Methylphenidate



- Used for apathy in AD
- 1 positive DB-RCT for apathy; functional status and depression
- Trend in cognition improvement (many studies)
- Might work if inattention is present (TBI)

Lithium



- Mice showed inhibitor of glycogen synthase Kinase-eB (blocks accumulation of AB peptides and also ↓ p-TAU and inflammation)
- Other mechanisms postulated
- 2 phase-II on-going
- More preventative than curative

Carbomazepine and Mirtazapine



- Both agents were positive in small open studies
- Large phase III, multi-center
- Mirtazapine can increase confusion and decrease memory

Mp101



- Phase II ongoing for treatment of dementia-psychosis
- Mitochondrial modulator via ↓ free radicals and ↑ BDNF

Oxytocin

- Lack of empathy
- ↑ prosocial behaviour
- 1 on-going RTC in FTD



Cyproterone

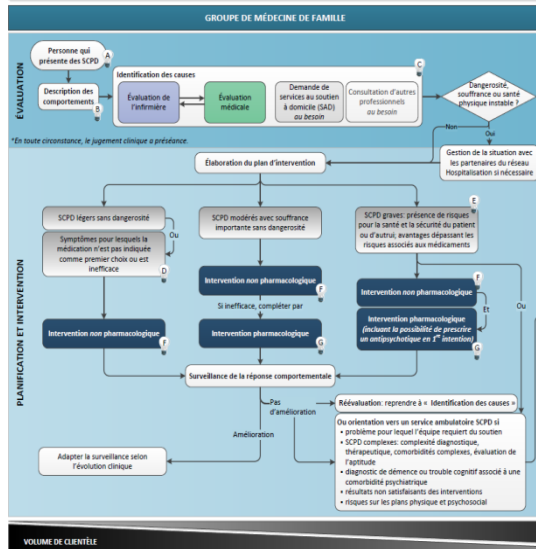


- Hypersexuality
- 1 positive DB-RCT for agitation/aggressivity in non-hypersexual pts – Huertas et al, 2007.
- 1 Meta-analysis positive (Bolea-Alamanac & al. 2011)

Medoxyprogesterone

- IM long acting
- Pedophilia
- To see
- Rare SE, CVA, Pulmonary embolism

PROCESSUS CLINIQUE GÉNÉRAL POUR LES PERSONNES ÂGÉES VIVANT À DOMICILE ET SUIVIES DANS UN GMF



Cligner sur les ombrages pour plus de détails ou référer-vous à la page indiquée par la lettre correspondante.

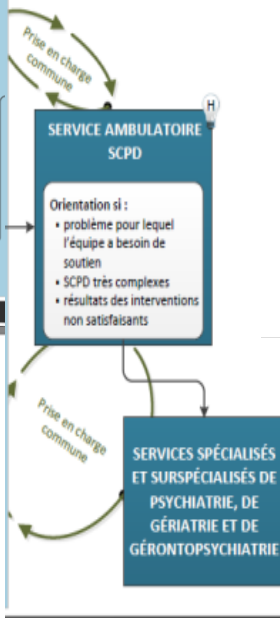
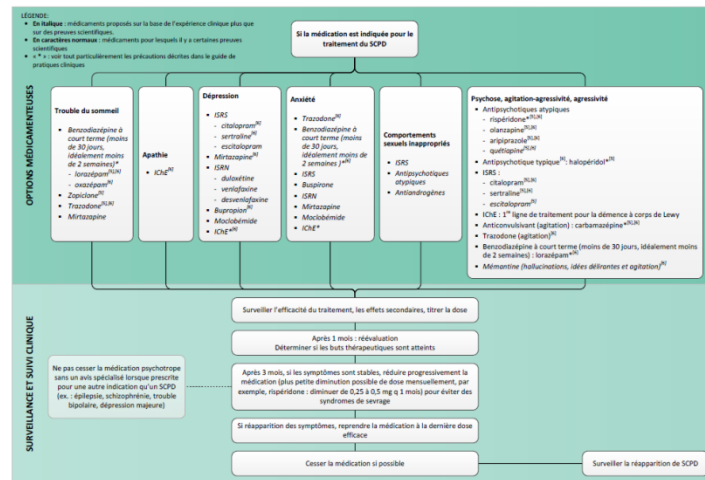


Schéma 2 : Approche pharmacologique pour les soins de première ligne

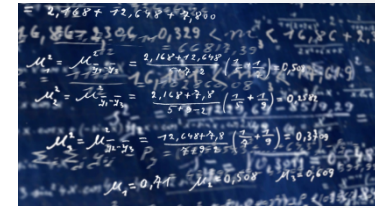


[5] D.P. Smitz, 2012; [6] IPA, 2012. Le présent schéma a été traduit et adapté à partir du document intitulé *Best Practice Guideline for Accommodating and Managing Behavioural and Psychological Symptoms of Dementia in Residential Care* (7).

Ministère de la Santé et des Services sociaux

Processus clinique
visant le traitement des symptômes comportementaux et psychologiques de la démence

Algorithm CAMH



- We participate as a center
- Wash-out 1 week
- 2 weeks – behavioural
- Risperidone
- Aripiprazole/Quiétiapine
- Carbamazepine
- Citalopram
- Gabapentin
- Prozosin
- Combination or ECT

Davies et al., Journal of Psypharmacology, 2018, Vol. 32 (5) 509 – 523.

House's Algorithm

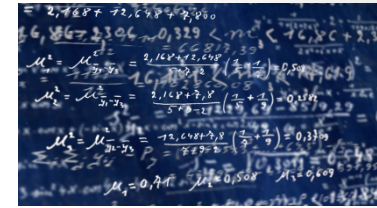
The image shows handwritten mathematical work for House's Algorithm. It includes the following steps and formulas:

$$M^0 = M_{\text{obs}}^0 = \begin{bmatrix} 2,464 & 7 & 2,648 & 2,460 \\ 6,867 & 3306 & 0,329 & 7,88 & 2,3 \\ 2,16 & 2,648 & 2,460 & 0,329 & 7,88 & 2,3 \\ 2,16 & 2,648 & 2,460 & 0,329 & 7,88 & 2,3 \end{bmatrix}$$
$$M^1 = M_{\text{est}}^1 = \frac{2,16 \times 2,648 \times 2,460}{2,16 \times 2,648 + 2,460 \times 2,16} = 0,508$$
$$M^2 = M_{\text{est}}^2 = \frac{2,16 \times 2,648 \times 2,460}{2,16 \times 2,648 + 2,460 \times 2,16} = 0,508$$
$$M^3 = M_{\text{est}}^3 = \frac{2,16 \times 2,648 \times 2,460}{2,16 \times 2,648 + 2,460 \times 2,16} = 0,508$$

At the bottom, the final estimated values are listed: $M_1 = 0,741$, $M_2 = 0,508$, and $M_3 = 0,609$.

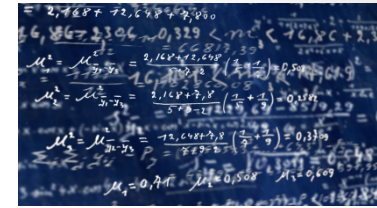
1. Physical
2. Akathisia
3. Sleep
4. Anxiousness
5. Depression
6. Psychosis

Principles



- ↓anticholinergic load
- Careful LVEF, Qtc, arrhythmia
- Pacemaker might be required
- eGFR, Na⁺
- Careful of EPS, falls and hypotension
- Discuss risks benefits of AA and off-label uses
- If unsuccessful, change meds
- If partial success, add meds
- Try to decrease and stop meds after 3-6 months (AA, etc...)
- Discuss ECT PRN

Suggested treatment



1. Escitalopram/Vortioxetine
2. Gabapentin/Pregabalin
3. Cyproterone/Progesterone
4. AA
5. Anticovulsivants
6. Oxytocin
7. Stimulants
7,5 rTMS, Tdcs
8. ECT
9. DBS

PRN's

- Loxapac and Ativan
- Loxapac
- Versed
- Propofol

