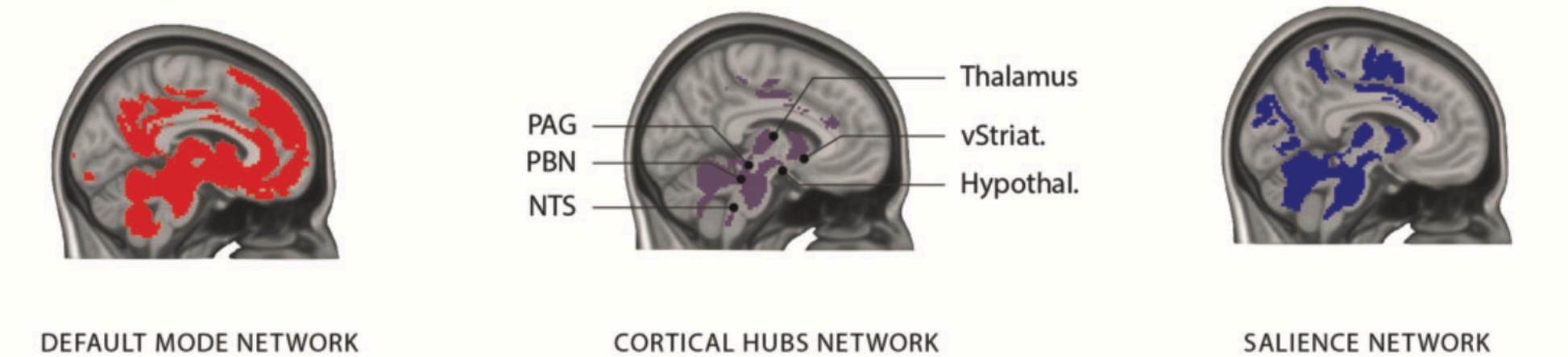
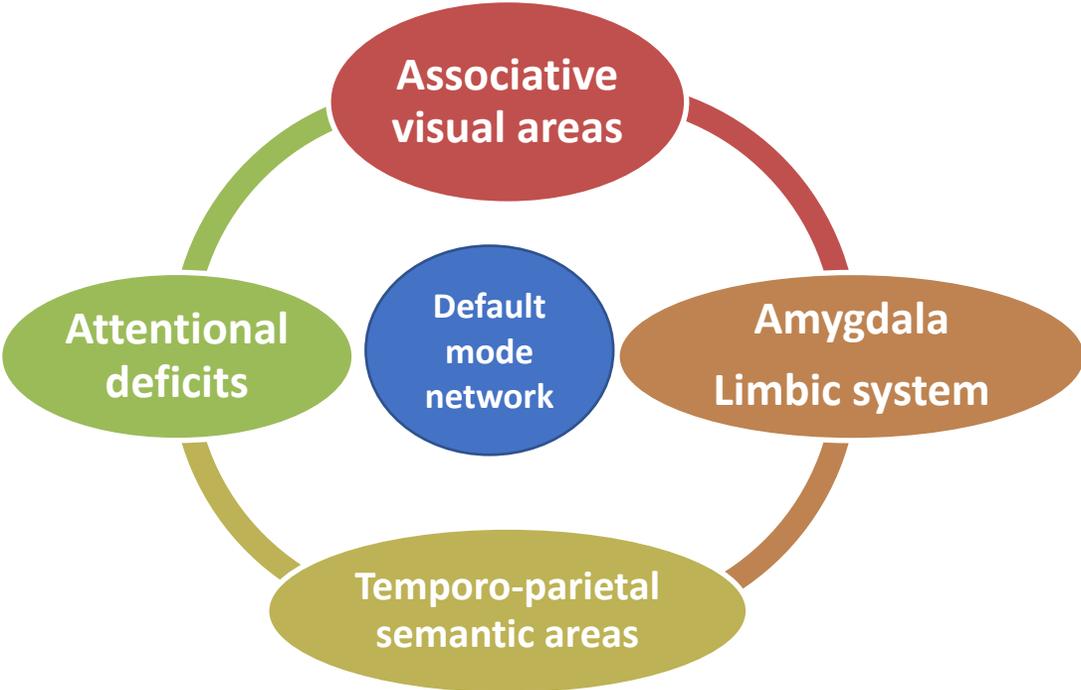


COVID, Sensory Deprivation and PD: Apathy and Behavioral Consequences



My personal experience during these months facing COVID ... (1)

& that of all PD patients that have been confined at their homes.

23 PD patients

- ✓ Advanced age >70 years.
 - ✓ Motor complications
- ✓ Personal history of anxiety-depressive disorder.
- ✓ Previous complaints of chronic pain.
 - ✓ Minor or mild hallucinations
 - ✓ Risk Factors → GBA mutations.
- ✓ Mild cognitive complaints or patients with mild dementia well-controlled before the pandemics.

Causal role of sensory deprivation, social isolation & loneliness ?

Psychosis

- ✓ Well-formed visual hallucinations.
 - ✓ Present daily.
- ✓ Loss of insight (continuous o during hallucinatory episodes).
- ✓ Confusional episodes with hallucinations during the transition from sleep to wakefulness
- ✓ Paranoid delusions with ideas of persecution, self-reference or delusional jealousy.

Anxiety > depressive syndrome +/- Apathy

- ✓ Panic attacks.
- ✓ Psychomotor agitation.
- ✓ Confusional episodes associated with increased anxiety.
- ✓ Recurrent and obsessive ideas regarding familial and personal fears

My personal experience during these months facing COVID ... (2)

& that of all PD patients that have been confined at their homes.

Huntington disease

- ❖ Three patients required permanent institutionalization because of nervous breakdown +/- irritability +/- cognitive and motor deterioration.
- ❖ Suicide attempt caused by intense anxiety related to the confinement.

PSP / Frontotemporal Demencia / Alzheimer's disease

- ❖ Inner restlessness, psychomotor agitation, generalizaed anxiety with panic attacks.
- ❖ Episodes of verbal and visual agression
(impossibility and prohibition to go out of home for a walk)

Loneliness and Social Isolation as Risk Factors for Mortality: A Meta-Analytic Review

Perspectives on Psychological Science
2015, Vol. 10(2) 227–237

Julianne Holt-Lunstad¹, Timothy B. Smith², Mark Baker¹, Tyler Harris¹, and David Stephenson¹

Type of measure	Description	Example of measure
Objective		
Social isolation	Pervasive lack of social contact or communication, participation in social activities, or having a confidant	Social Isolation Scale (Greenfield, Rehm, & Rogers, 2002) Social Network Index (bottom quartile; Berkman & Syme, 1979)
Living alone	Living alone versus living with others	Binary item: yes, no Number of people in household
Subjective		
Loneliness	Feelings of isolation, disconnectedness, and not belonging	Loneliness Scale (De Jong-Gierveld & Kamphuis, 1985) UCLA Loneliness Scale (Russell, Peplau, & Cutrona, 1980)

Characteristic	<i>M</i>	Number of studies (<i>k</i>)
Year of initial data collection	1,993	46
Years of participant follow-up	7	70
% deceased by the end of data collection	24.7	66
% female	52.6	67
Age of participants ^a	66.0	
<50 years		8
50–59 years		12
60–69 years		11
70–79 years		21
>80 years		10

Heikkinen and Kauppinen 2004 ;Patterson and Veenstra 2010; Steptoe et al. 2013.

Mortality

↓ Physical & Mental Health
Emotional well-being

Depression

Cognitive Impairment

↑ **Mortality Risk (Multivariate Analysis)**

29% Social Isolation

26% Subjective feeling of loneliness

32% Living Alone

Psychopathological Effects of Solitary Confinement

Stuart Grassian, M.D.

Am J Psychiatry 140:1450–1454, 1983

Psychopathological reactions to solitary confinement were extensively described by nineteenth-century German clinicians. In the United States there have been several legal challenges to the use of solitary confinement, based on allegations that it may have serious psychiatric consequences. The

present article describes clinical observations of 14 prisoner plaintiffs in a lawsuit alleging that the conditions they were exposed to in solitary confinement were violations of Eighth Amendment protection against “cruel and unusual punishment.”

Charles Darwin (1876) *“Inmates were dead to everything but torturing anxieties and horrible despair ... forgetting daily situations and staring at strange visions (8, p. 66).”*

Freedman, S. & Greenblatt, M. (1960). "Studies in Human Isolation IV: **Hallucinations** and Other Cognitive Findings." U.S. Armed Forces Medical Journal, 11, 1479-1497.

Gunderson, E.K. (1963). **Emotional symptoms** in extremely isolated groups. Archives of General Psychiatry, 9, 362-368.

Cochrane, J.J., & Freeman, S.J.J., (1989). Working in **Arctic and sub-arctic** conditions: Mental health issues. Canadian Journal of Psychiatry, 34, 884-890.

Psychopathological Effects of Solitary Confinement

Stuart Grassian, M.D.

Am J Psychiatry 140:1450–1454, 1983

Confinement in a prison cell **with no windows**, just one door with a small window
with no natural light and proper air circulation

Mean time of confinement --- **2 months (range 11 days --- 10 months)**.

- ✓ **Generalized hyperresponsivity to external stimuli** → annoying and even unbearable increase of common sensory stimuli (noise, smell of food, light).
- ✓ **Perceptual distortions and hallucinations** → Visual illusions, auditory and structured visual hallucinations.
- ✓ **Affective Disturbances** → Severe anxiety with generalized anxiety disorder and panic attacks with depersonalization and derealization.
- ✓ **Difficulties With Thinking, Concentration, and Memory** → Inattention, recurrent confusional states, memory loss → “I can't concentrate, can't read. . . . My mind is narcotized... My memory is going. “
- ✓ **Disturbances of Thought Content** → Aggressive egodystonic intrusions, paranoid and self-referential delusional ideation.
- ✓ **Problems With Impulse Control** → Emotional responses and irrepressible behaviors with negative consequences → Physical aggression, psychomotor agitation.

Emotional Symptoms in Extremely Isolated Groups

E. K. ERIC GUNDERSON, PhD
SAN DIEGO, CALIF

ARCHIVES OF GENERAL PSYCHIATRY

Arch Gen Psychiatry. 1963; 9: 362-368.

Hebb,³ in his experimental work on what he called perceptual isolation, suggested that monotonous sensory stimulation produces a disruption of the capacity to learn or even to think. Hebb's associates, Heron,⁴ Bexton, Scott, and Doane, found that with greatly reduced amount and patterning of sensory input, their volunteers experienced inability to think or concentrate, anxiety, somatic complaints, temporal and spatial disorientation, visual phenomena described as hallucinations, and deficits in task performance.

During their confinement in the experimental cubicles, subjects evidenced boredom, restlessness, anger, stress, anxiety, disorientation, and vague physical symptoms that were rarely reported in controls.

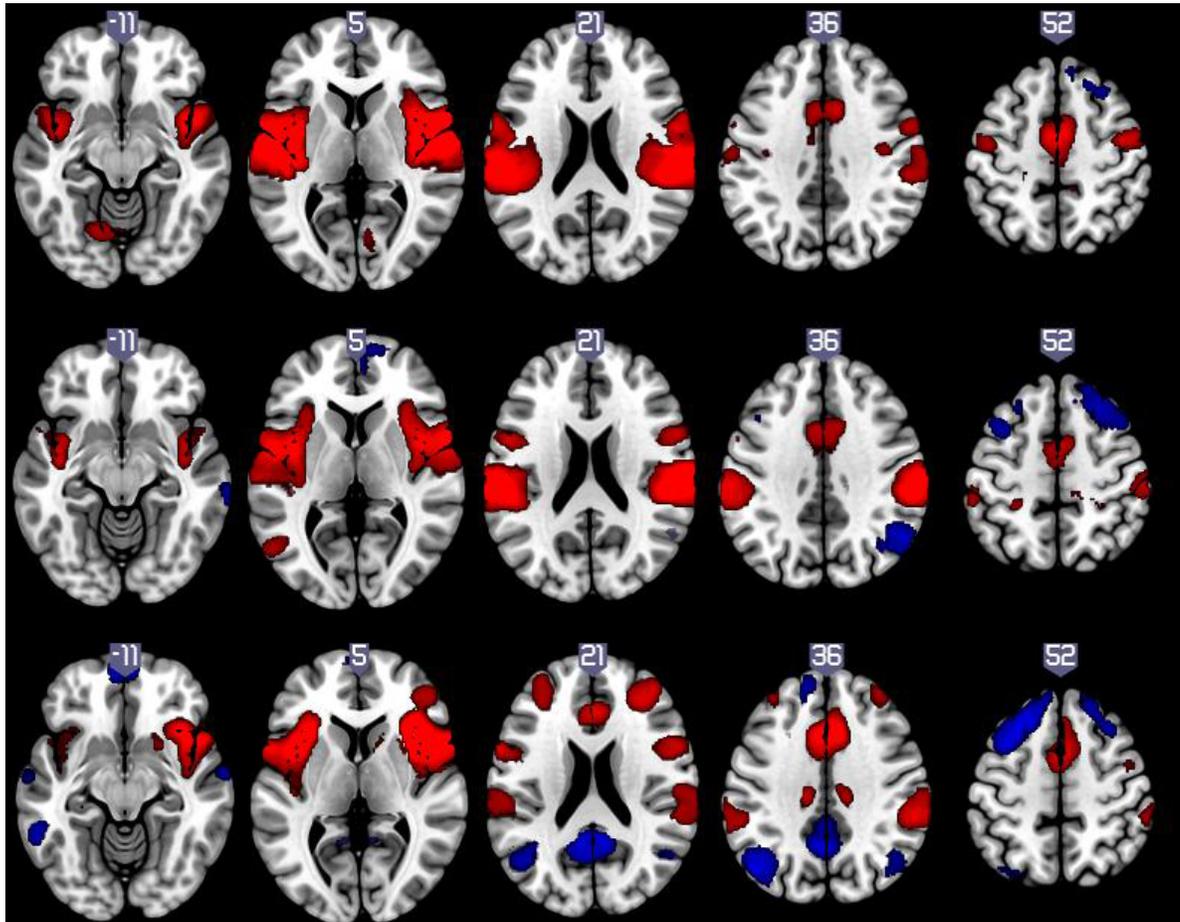
During the International Geophysical Year of 1957 and 1958, twelve nations carried out an extensive cooperative scientific program in Antarctica. As part of its contribution, the United States established seven year-round bases on the Antarctic continent.

	1st	2nd	3rd
Sleep disturbances:			
Difficulty falling asleep or staying asleep	34 †	72	54
Waking up at night	31 †	58	49
Depression:			
Feeling blue	34 †	56	42
Feeling lonely	28 *	37	35
Feeling people were watching or talking about you	8	11	11
Preferring to be alone ‡	21 *	28	21
Being quiet and sad at parties			
Aggression:			
Feeling easily annoyed or irritated	35 *	49	46
Feeling critical of others	35 *	49	49
Finding others short-tempered or unkind	14 †	30	39
Burning up with anger			
	N	112	177
Anxiety:			
Sudden fright for no apparent reason	4	7	8
Bad dreams	6 *	18	20
Nervousness and shakiness under pressure	14	18	22
Feeling uneasy without knowing why	14	22	17
Sudden noises making you jump			
Difficulty in making up your mind			

Perceived Social Isolation is Associated with Altered Functional Connectivity in Neural Networks Associated with Tonic Alertness and Executive Control

Elliot A. Layden, John T. Cacioppo, Stephanie Cacioppo, Stefano F. Cappa, Alessandra Dodich, Andrea Falini, Nicola Canessa

NeuroImage 20 September 2016



Loneliness (Perceived Social Isolation)



↑ **Connectivity**
cingular-lymbic-
opercular circuits

↓ **Connectivity**
fronto-parietal
(DAN/CEN)
networks



↑ **Alert**, hyperarousal,
social fears and
perception of threats

Attentional and
executive dysfunction

*'Hypervigilance to
social threat'*

↓ *'Goal-directed
attention'*

Sensory Deprivation and Hallucinations

What conditions of minimal or controlled sensory stimulation favor the generation of hallucinations?

Jack Vernon, Theodore Marton, Ernest Peterson



SCIENCE, VOL. 133 9 JUNE 1961

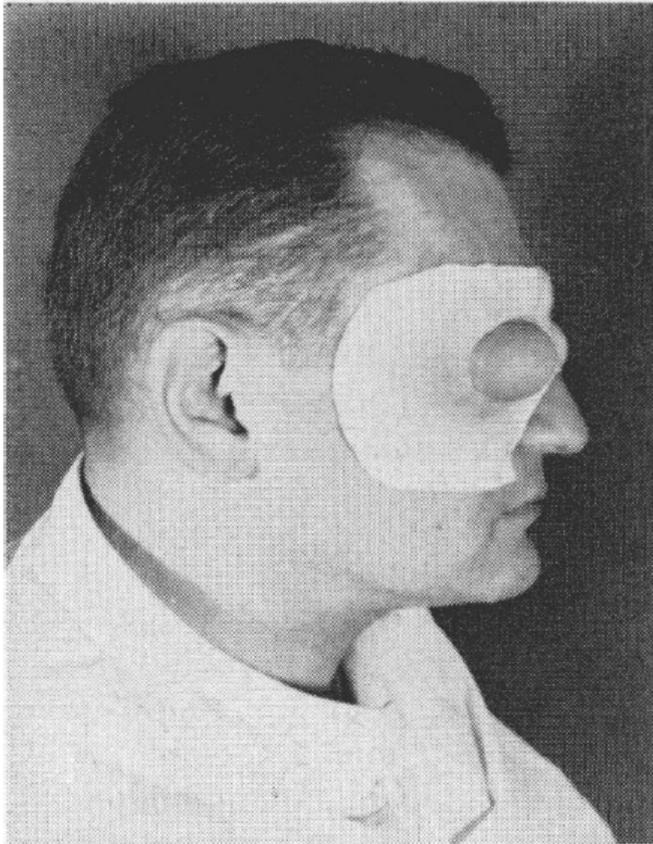


Fig. 1. Shaped ping-pong balls attached over a subject's eyes by mole skin.



Fig. 4. A posed picture showing a subject's position in the cubicle and the arrangement of food and water (the subject would not wear a wrist watch in an actual study). The microphone hanging from the ceiling is for monitoring.

Sensory Deprivation and Hallucinations

SCIENCE, VOL. 133 9 JUNE 1961

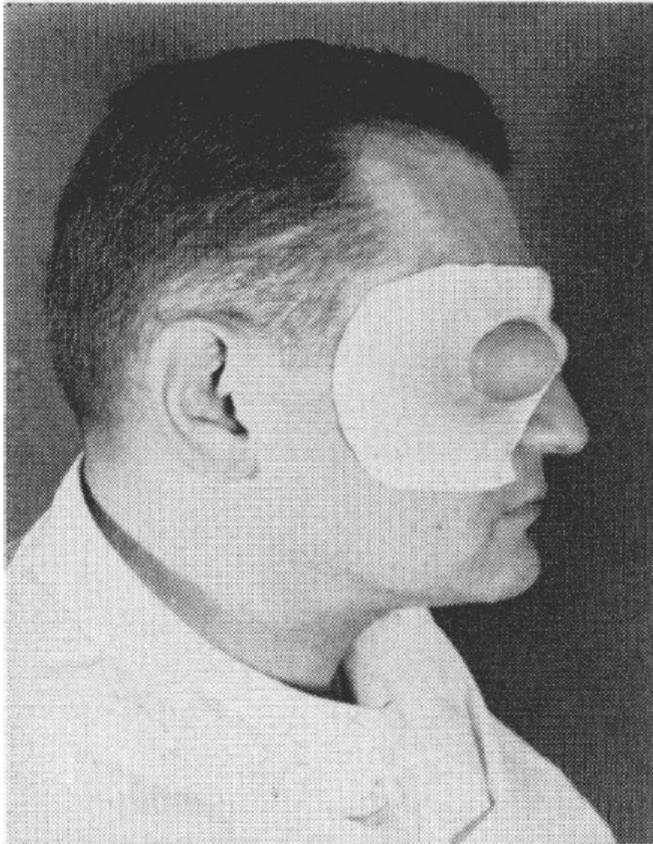


Fig. 1. Shaped ping-pong balls attached over a subject's eyes by mole skin.

What conditions of minimal or controlled sensory stimulation favor the generation of hallucinations?

Jack Vernon, Theodore Marton, Ernest Peterson

McGill et al. → Social Isolation/Confinement of **29 young and Healthy volunteers**

Developed hallucinations in different sensory modalities (visual, auditory, tactile) in 20/29 participants after 20-70 hours of lockdown.

Silent and quiet room in dim light for 72 hours

10/14 young and healthy volunteers developed hallucinations

- ✓ 5/10 Simple and Mild hallucinations (lights, simple lines, illusions of movement in the periphery of the visual field).
- ✓ 2/10 Complex hallucinations (geometrical figures, formed figures in the center of the visual field identified either as people, animals or objects).
- ✓ 3/10 Very well-structured and persistent visual, auditory and tactile hallucinations

Science

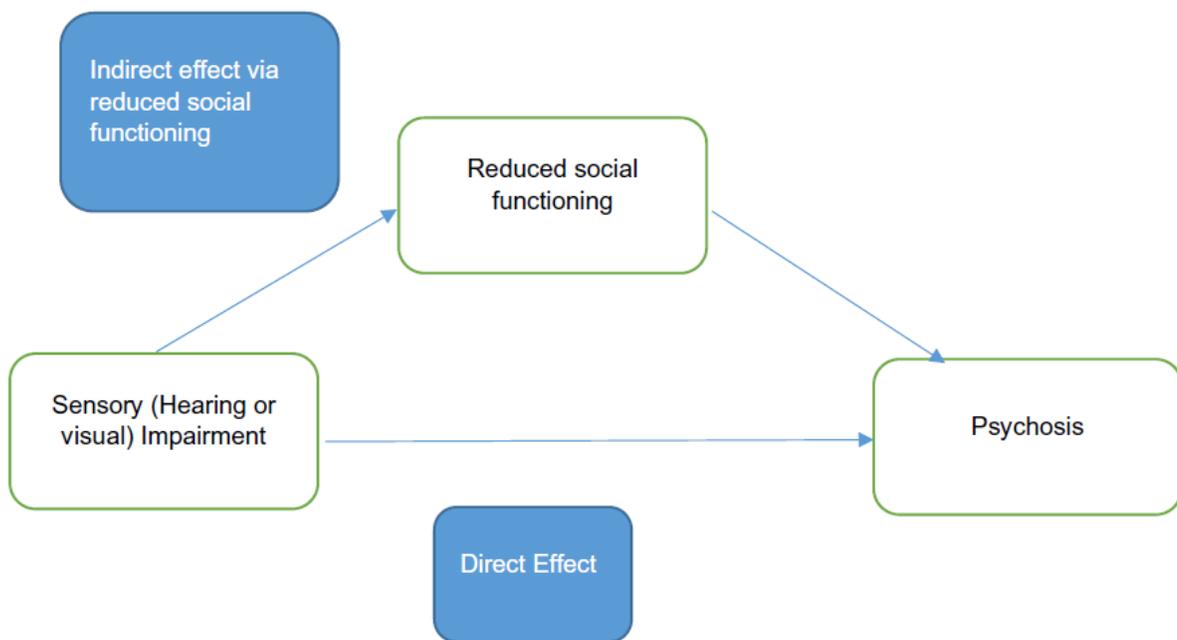
AAAS

Psychotic symptoms and sensory impairment: Findings from the 2014 adult psychiatric morbidity survey☆

Natalie Shoham ^{a,*}, Gemma Lewis ^a, Joseph Hayes ^a, Sally McManus ^b, Reza Kiani ^c, Traolach Brugha ^c, Paul Bebbington ^a, Claudia Cooper ^a

Odds ratios with 95% confidence intervals for screening positive on the Psychosis Screening Questionnaire (PSQ) according to presence of hearing and visual impairment.

Type of sensory impairment n = 7107	Unadjusted Odds Ratio relative to no difficulty (95% CI)	p-Value	Adjusted ^a Odds Ratio relative to no difficulty (95% CI)	p-Value
Hearing impairment	0.98 (0.74 to 1.31)	0.911	1.50 (1.10 to 2.04)	0.010
Visual impairment	1.68 (1.26 to 2.24)	<0.001	1.81 (1.33 to 2.44)	<0.001



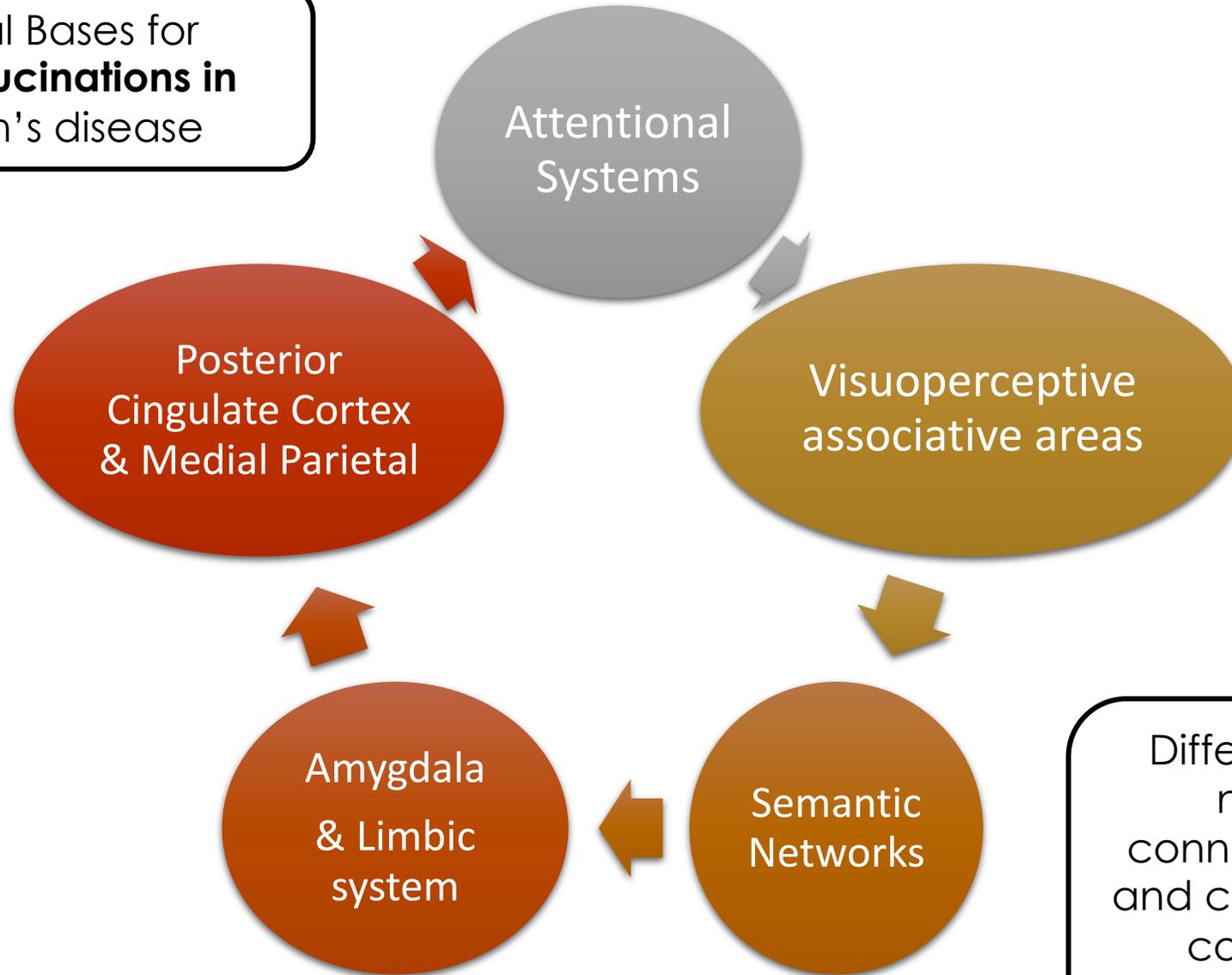
- Psychosis Screening Questionnaire (PSQ)
 - Hallucinations & Delusional Ideas.
- The Social Functioning Questionnaire (SFQ)

Visual Impairment → ↑ Hallucinations & Delusions
 ↓ Hearing → ↑ Delusional Ideas (persecution and self-referential)

Social Isolation

Independent Variable with an additional effect on the development of hallucinations and delusions in elderly ‘healthy’ population.

Neuronal Bases for
visual hallucinations in
Parkinson's disease



Different **complex networks** need to be precisely connected in order to quickly and correctly "**understand**" the constant and **changing environmental stimuli**

The Brain's Default Network

Ann. N.Y. Acad. Sci. 1124: 1–38 (2008)

Anatomy, Function, and Relevance to Disease

RANDY L. BUCKNER,^{a,b,c,d,e} JESSICA R. ANDREWS-HANNA,^{a,b,c}
AND DANIEL L. SCHACTER^a

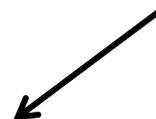
Attention towards *internal*
mental processes



DMN activation



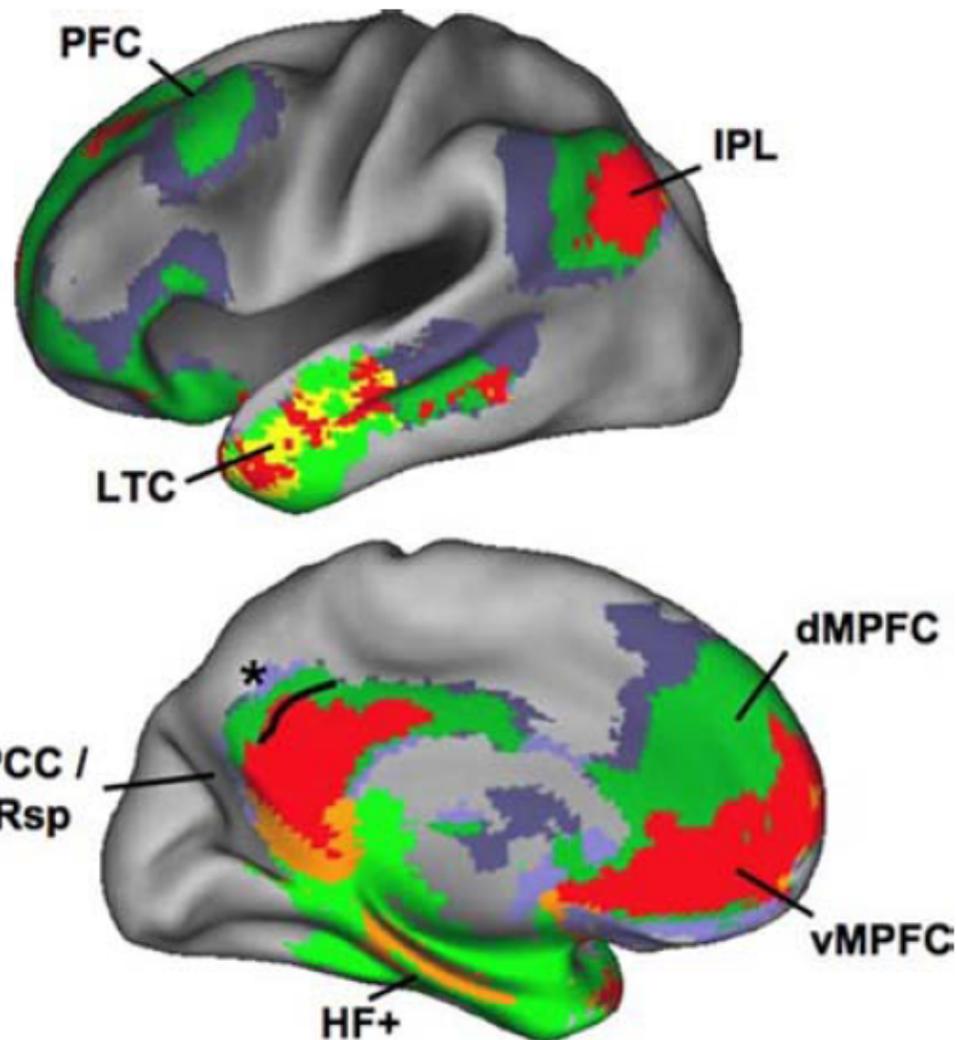
DMN deactivation



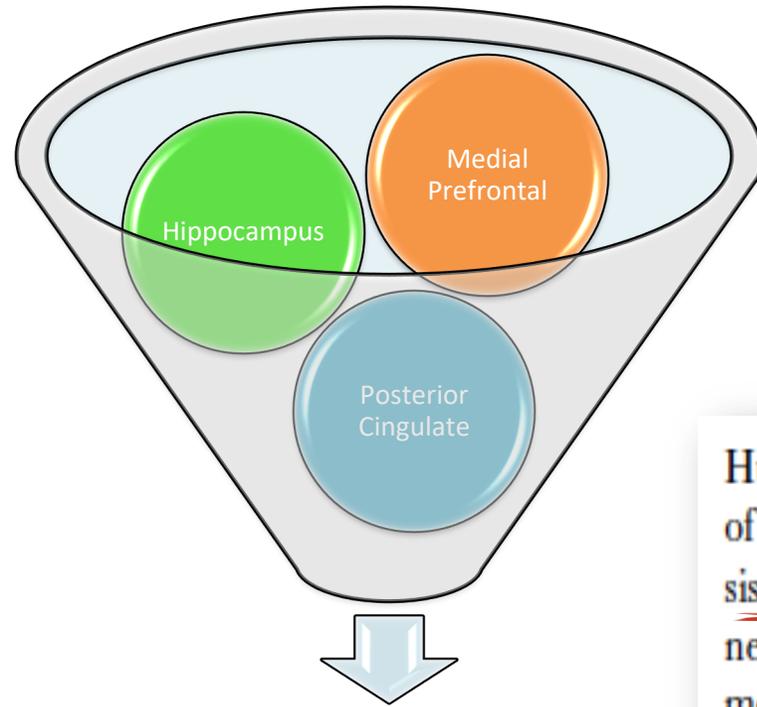
Anticorrelated activity
with the DAN & VAN



Attention towards *external*
environmental stimuli



Default mode network (DMN)



*Life Simulator
Verbal & Visual
Imagery*

Human beings spend nearly all of their time in some kind of mental activity, and much of the time their activity consists not of ordered thought but of bits and snatches of inner experience: daydreams, reveries, wandering interior monologues, vivid imagery, and dreams. These desultory concoctions, sometimes unobtrusive but often moving, contribute a great deal to the style and flavor of being human. Their very humanness lends them great intrinsic interest; but beyond that, surely so prominent a set of activities cannot be functionless. (Klinger 1971 p. 347)



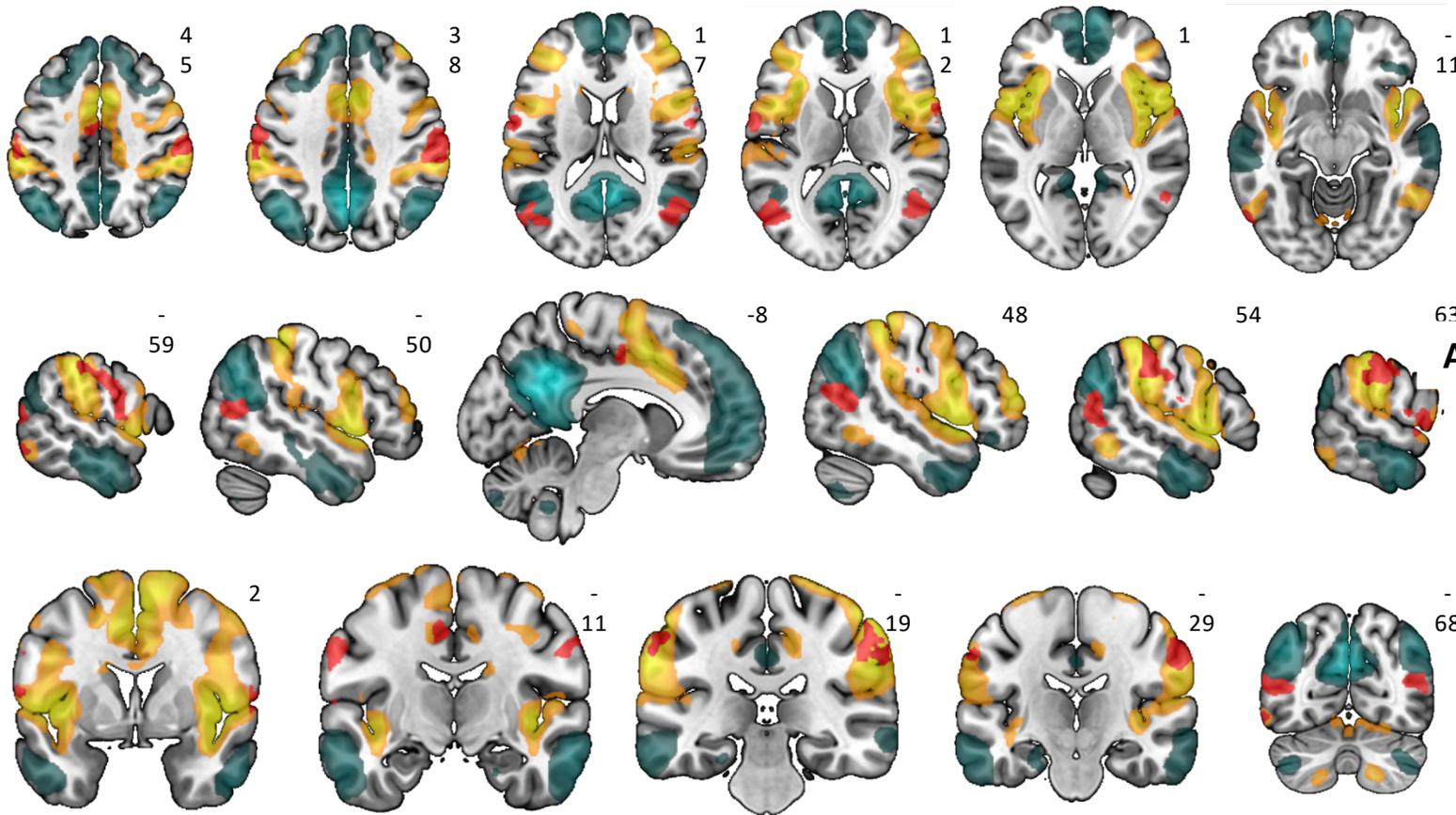
Disruption of the Default Mode Network and Its Intrinsic Functional Connectivity Underlies Minor Hallucinations in Parkinson's Disease

Helena Bejr-kasem, MD,^{1,2,3,4} Javier Pagonabarraga, MD, PhD,^{1,2,3,4*} Saül Martínez-Horta, BSc,^{1,2,3,4}
 Frederic Sampedro, PhD,^{3,4} Juan Marín-Lahoz, MD,^{1,2,3,4} Andrea Horta-Barba, BSc,^{1,3,4} Ignacio Aracil-Bolaños, MD,^{1,3,4}
Movement Disorders, Vol. 34, No. 1, 2019

Group differences between PD-mH and PD-NH in PCC functional connectivity (rs-fMRI)



Decreased connectivity with prefrontal **attentional** areas, and anterior temporal areas involved in **high-level visual processing**



	Brain region	BA
Attention	Superior frontal gyrus	8
	Middle frontal gyrus	6
Visual processing	Inferior temporal gyrus	20
	Inferior temporal gyrus	20
	Superior frontal gyrus	8
	Temporal pole	38
	Superior frontal gyrus	8

* Cluster level FWE corrected. $p < 0.05$

Hallucinations, loneliness, and social isolation in Alzheimer's disease

COGNITIVE NEUROPSYCHIATRY, 2016
<http://dx.doi.org/10.1080/13546805.2015.1121139>

Mohamad El Haj, Renaud Jardri, Frank Larøi & Pascal Antoine

		AD (n = 22)	Controls(n = 24)
Percentage of women		72.72%	62.5%
Age (years)		71.55 (5.71) ^{n/s}	68.17 (7.74)
Education (years)		8.50 (2.63) ^{n/s}	9.83 (2.99)
General Cognitive functioning	Mini-Mental State Examination	21.73 (1.80) ^{***}	28.08 (1.47)
Episodic memory	Grober and Buschke	6.00 (2.50) ^{***}	10.96 (3.40)
Working memory	Forward span	4.05 (1.17) ^{***}	6.29 (1.43)
	Backward span	3.36 (1.22) [*]	4.13 (1.65)
Verbal Fluency	Fluency task (letter P)	17.77 (5.56) ^{***}	23.67 (5.22)
Depression	Hospital Anxiety and Depression Scale	10.68 (2.57) ^{***}	7.79 (2.22)

Regression Analysis

“**Social isolation** was the only variable contributing significantly to hallucinations in **AD** participants ($\beta = 0.53, p < 0.05$) and healthy **controls** ($\beta = 0.51, p = 0.01$).

Table 3. Correlational matrix for hallucinations, loneliness, and social isolation in AD and healthy control participants.

		Hallucinations	Loneliness	Social isolation
AD	Hallucinations	–		
	Loneliness	$p = .01$	–	
	Social isolation	$p < .01$	$p < .001$	–
Controls	Hallucinations	–		
	Loneliness	$p = .011$	–	
	Social isolation	$p < .01$	$p < .001$	–

Note: All correlational coefficients are significant after applying a Bonferroni correction (threshold of $p < .017$).

The theory of constructed emotion: an active inference account of interoception and categorization

Social Cognitive and Affective Neuroscience, 2017, 1–23

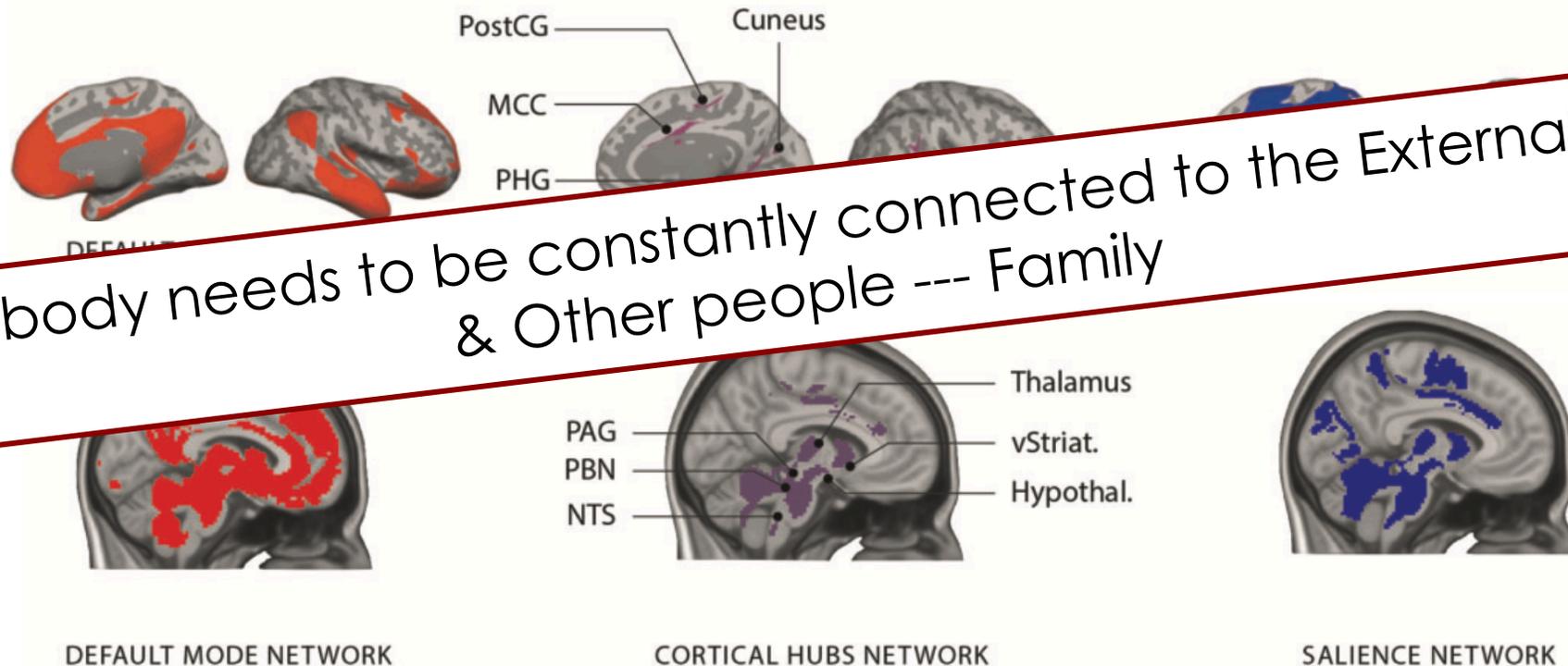
Lisa Feldman Barrett^{1,2,3}

“Large-scale network” & Emotional Control

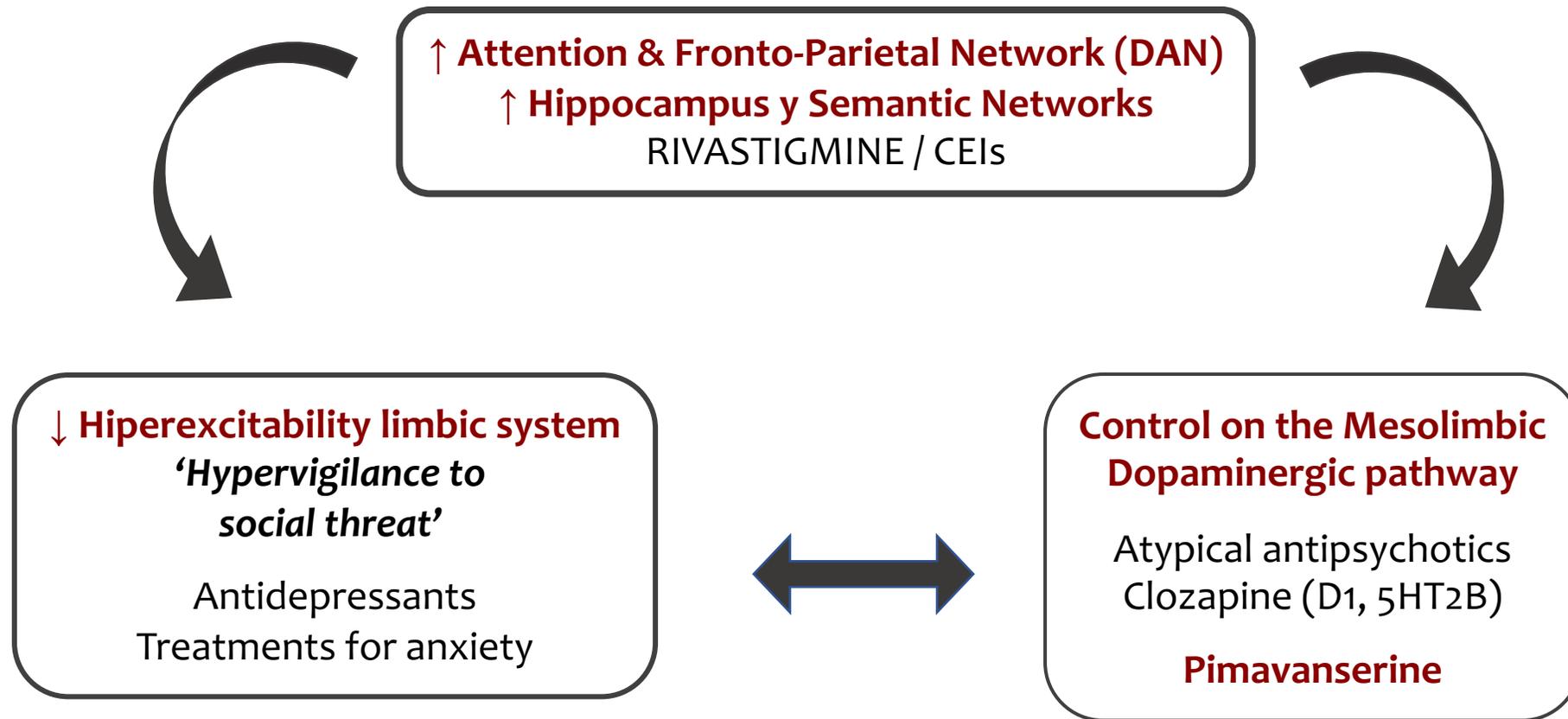
Regulation of **“spontaneous emotions”** is anticipated by **pre-conscious body signals/sensations** Elicited by external stimuli & activity of core centers of emotion generation (limbic system/amygdala)



Global unconscious response involving emotional-cognitive-motor behaviors



Our body needs to be constantly connected to the External world & Other people --- Family



Psychotherapy & NON pharmacological treatments

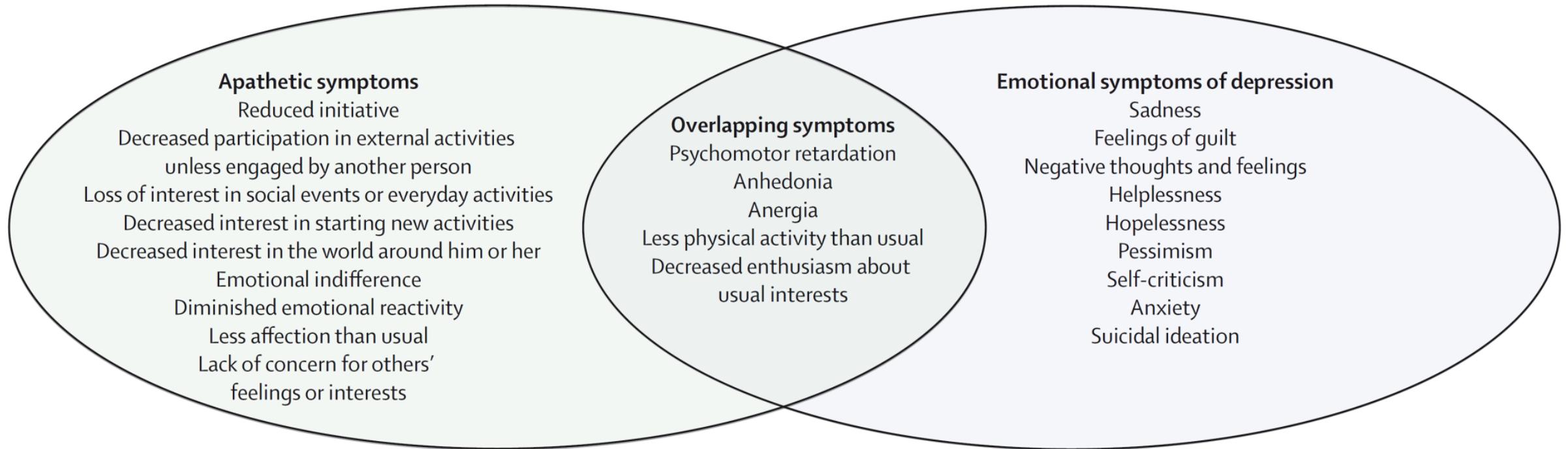
NEED for Orienting Environmental Stimuli

There is a need for patients with neurodegenerative diseases to go out and maintain family contact
Well-illuminated, diaphanous and clean rooms & different cues about the time of the day.

Apathy in Parkinson's disease: clinical features, neural substrates, diagnosis, and treatment

Lancet Neurol 2015; 14: 518–31

Javier Pagonabarraga, Jaime Kulisevsky, Antonio P Strafella, Paul Krack

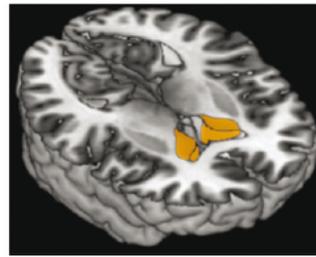


The constant flow of past and incoming information within the **emotional brain (limbic system)** is transferred first to the frontal lobe, and then to preparatory motor areas.

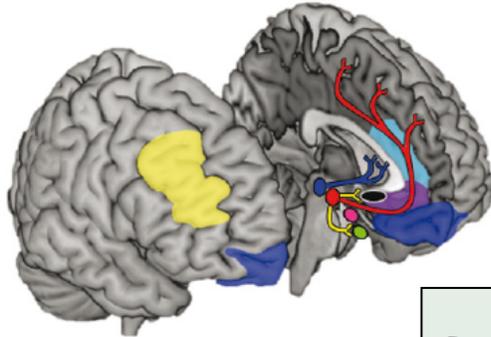
Apathy, defined as a state of diminished **goal-directed behaviors**, can be the consequence of **cognitive problems, depression** or **difficulties in experience pleasure** (anhedonia) in response to external stimuli.

Apathy in Parkinson's disease: clinical features, neural substrates, diagnosis, and treatment

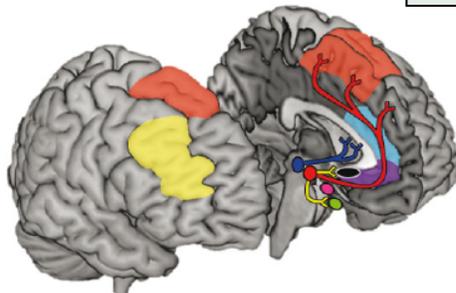
<https://www.movementdisorders.org/MDS/Scientific-Issues-Committee-Blog/Apathy-in-Parkinsons.htm>



A Emotional-affective apathy

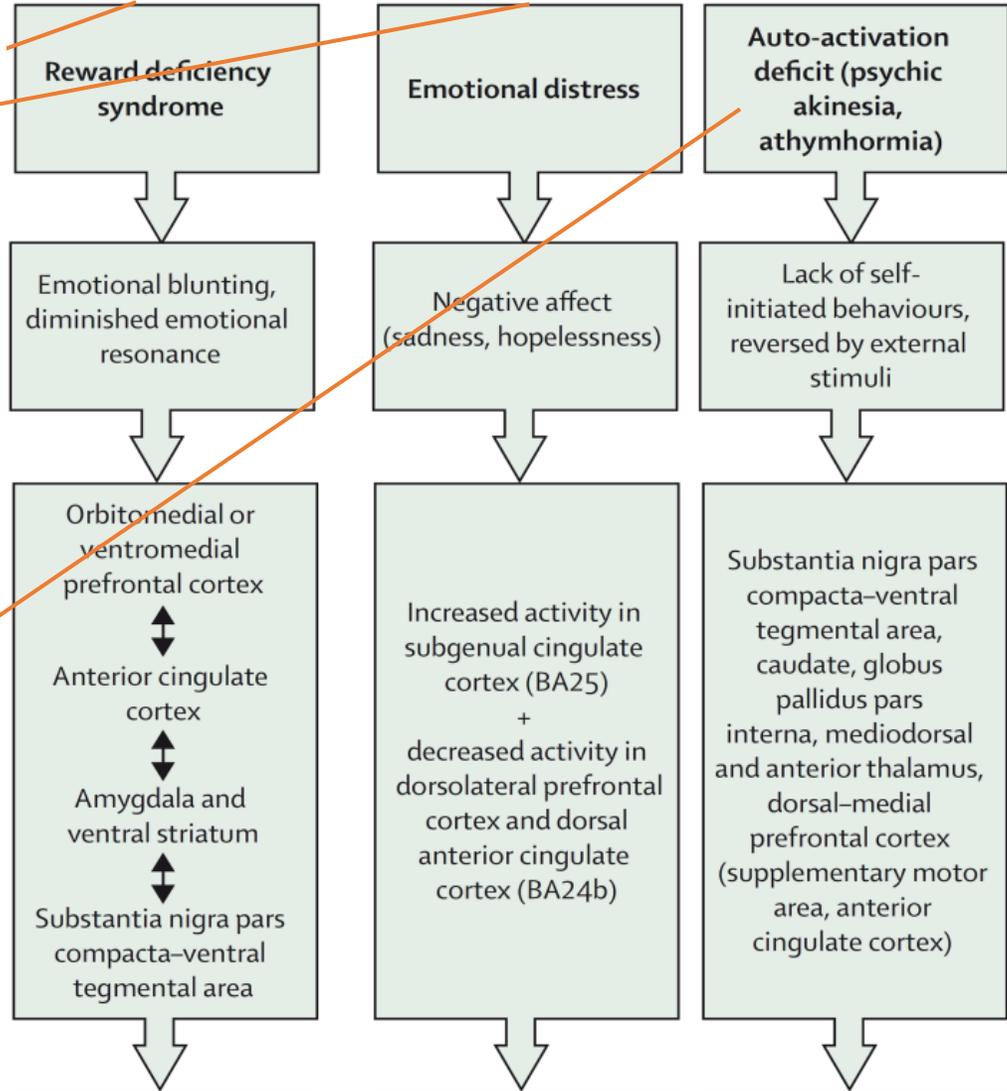


C Auto-activation apathy



Antidepressants (SNRIs, bupropion, tetracyclic antidepressants, tricyclic antidepressants)

Dopamine receptor agonists



➤ How can we then differentiate apathy from depression?

*Differentiation of apathy from depression is mainly based on a well-structured clinical interview...
... But ALSO on being aware of our inner feelings and to prepare the visits to the neurologist or psychologist
so they can understand better all the difficulties that Parkinson's disease may cause in daily life*

Depression -- enhancement of negative thoughts, beliefs and emotions

- ✓ Emotional symptoms of depression → Increased sadness, feelings of guilt, recurrent and even involuntary intrusion of negative feelings, helplessness, hopelessness, anxiety, and even suicidal ideation.
- ✓ Cognitive symptoms of depression recurrent and involuntary intrusion of negative thoughts (negative ruminations), pessimism, self-criticism.

Apathy -- It is noteworthy that while in depression patients are able to explain sadness as the source of their inactivity, apathetic patients are no longer able to understand which is the origin of that progressive development of decreased interest in the world around them.

- ✓ Spontaneous reduction of interests, activities and emotions.
- ✓ Decreased participation in external activities (unless engaged by another person).
- ✓ Loss of interest in social events or everyday activities.
- ✓ Emotional indifference, less affection than usual, or lack of concern for others' feelings or interests.

Conclusions

- [1] In some patients WE HAVE NOT given a proper response when needed
→ We must learn the lesson for the future!
- [2] The management of social isolation, sensory deprivation and loneliness in patients with neurodegenerative diseases is not only important during the pandemics BUT ALSO in the usual control of our patients.
- [3] Depression, anxiety and apathy must be carefully distinguished and interpreted by patients, caregivers and physicians in order to manage them correctly, either with medications and with different social and psychological interventions.