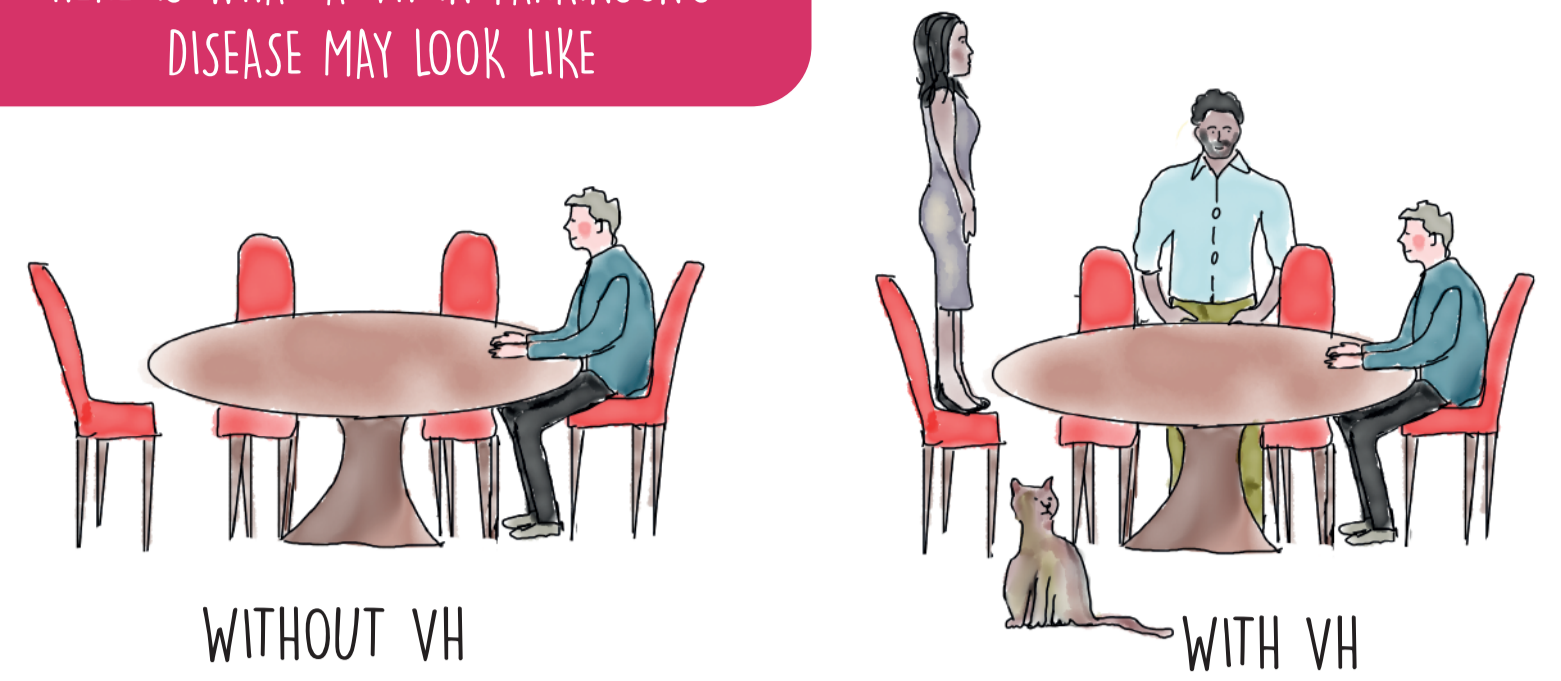


SHEDDING A LIGHT ON VISUAL HALLUCINATIONS IN PARKINSON'S DISEASE

PEOPLE WITH PARKINSON'S (PWP) LOSE NEURONS IN MULTIPLE BRAIN REGIONS. AS A RESULT, PWP EXPERIENCE ABNORMALITIES AND A DISBALANCE IN KEY NEUROTRANSMITTER PATHWAYS WHICH – IN AN INTERPLAY WITH MEDICATION – MAY LEAD TO VISUAL HALLUCINATIONS (VH)

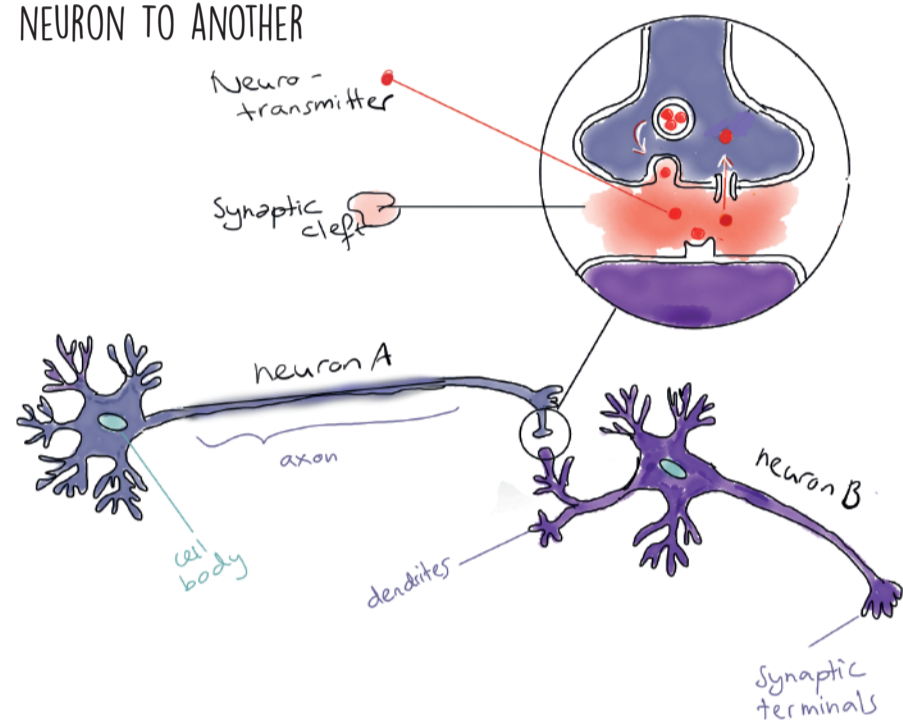
HERE IS WHAT A VH IN PARKINSON'S DISEASE MAY LOOK LIKE



JUST A FEW BASIC CONCEPTS FIRST

NEURONS AND NEUROTRANSMITTERS

NEUROTRANSMITTERS TRANSMIT SIGNALS ACROSS THE SYNAPTIC CLEFT FROM ONE NEURON TO ANOTHER

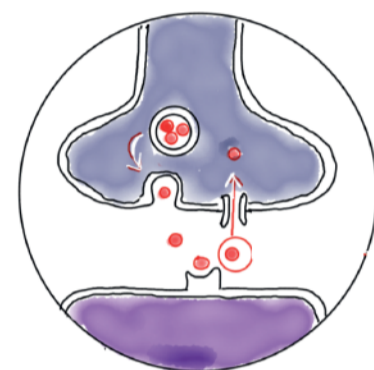


A NEURON IS A SPECIALIZED CELL – A NERVE CELL – DESIGNED TO TRANSMIT INFORMATION TO OTHER CELLS

AGONISTS AND ANTAGONISTS

A NEUROTRANSMITTER (E.G. DOPAMINE) FITS INTO THE CORRESPONDING RECEPTOR AND ACTIVATES IT TO TRANSMIT A SIGNAL.

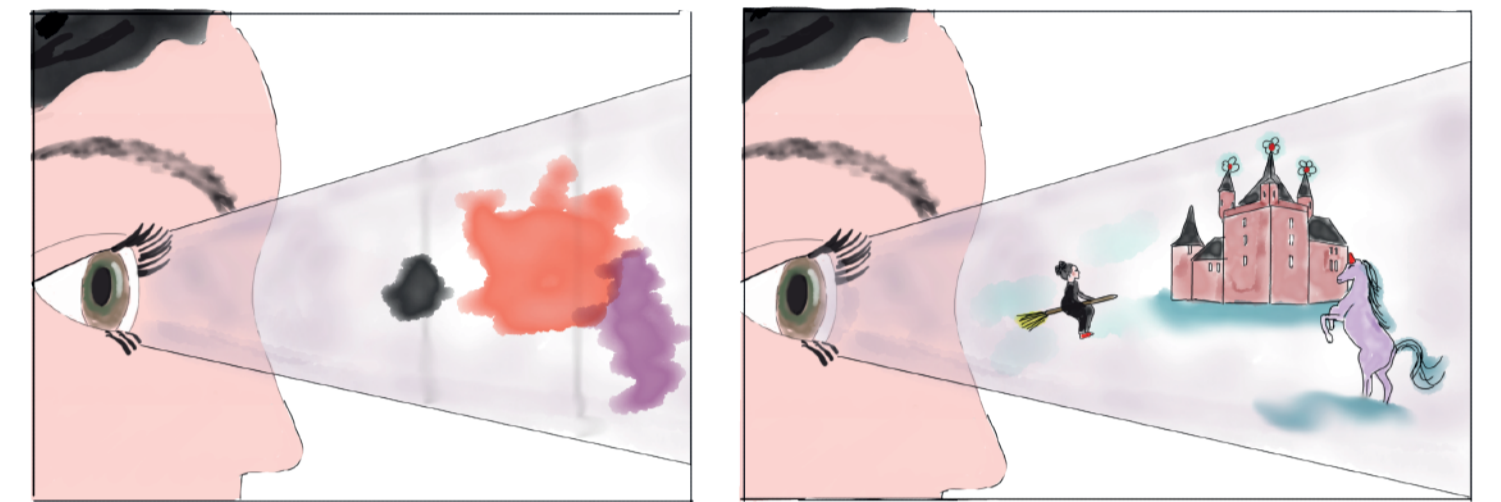
- dopamine
- Ⓜ dopamine receptor
- Ⓜ dopamine transporter



AN AGONIST IS A NEUROTRANSMITTER LOOK-A-LIKE. IT MIMICS ITS ACTION WITHOUT BEING THE NEUROTRANSMITTER ITSELF. AN INVERSE AGONIST FITS THE RECEPTOR AND ELICITS THE OPPOSITE ACTION. AN ANTAGONIST BLOCKS THE RECEPTOR WITHOUT ELICITING ANY ACTION.

A CONCEPTUAL MODEL FOR VH IN PARKINSON'S DISEASE (PD)

IN PD PART OF OUR ATTENTIONAL NETWORKS DEGENERATE, LEADING TO DYSFUNCTIONAL NETWORK INTERACTIONS AND FAULTY PROCESSING OF INFORMATION LEADING TO FALSE PERCEPTIONS.

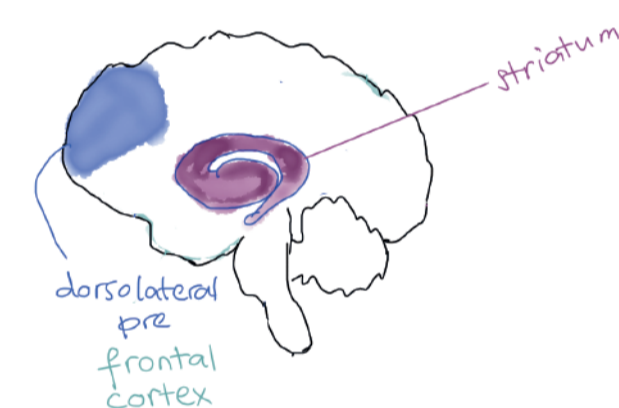


IN CASE OF AMBIGUOUS VISUAL INPUT AND A FAILURE TO ENGAGE THE DORSAL ATTENTION NETWORK (DAN)

IMAGERY IS REPLACED WITH IMAGERY FROM THE DEFAULT MODE NETWORK (DMN)

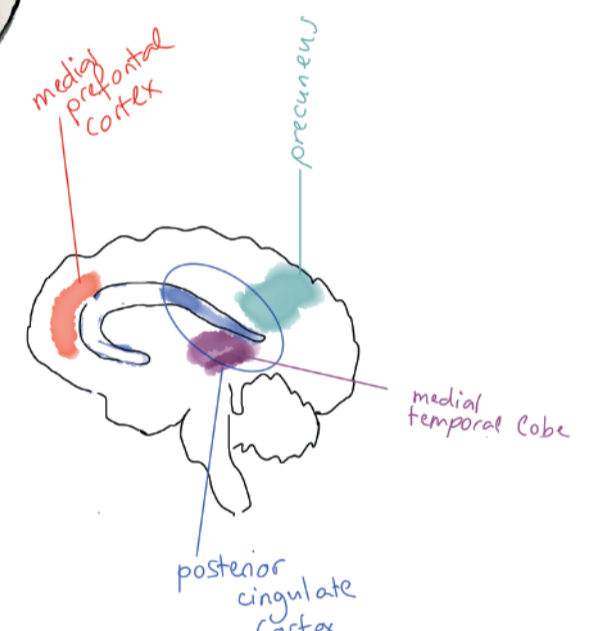
WHAT ARE DAN AND DMN? WE WILL ANSWER THIS QUESTION WITH A SAGGITAL INTERSECTION OF THE BRAIN

DAN



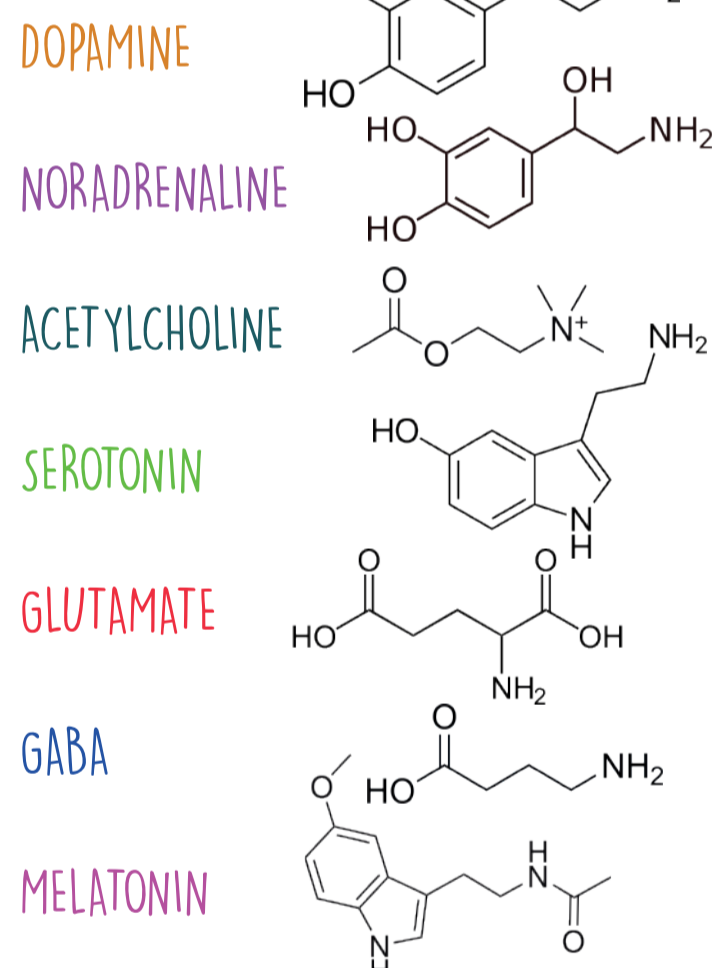
THE DAN IS RESPONSIBLE FOR A GOAL-DIRECTED RESPONSE TO EXTERNAL STIMULI

DMN



THE DMN FUNCTIONS ARE OUR DEFAULT MODE OF ATTENTIONAL PROCESSING IN A STATE OF REST. ITS FUNCTION IS INTROSPECTION, EPISODIC MEMORY AND MIND WANDERING

7 KEY NEUROTRANSMITTERS ...



LEVODOPA IS A PRECURSOR TO DOPAMINE AND IS OFTEN PRESCRIBED FOR PD. ADVANCED THERAPIES SUCH AS DEEP BRAIN STIMULATION, APOMORPHINE AND LEVODOPA CARBIDOPA INTESTINAL GEL REDUCE VH, POSSIBLY BECAUSE LOWER LEVELS OF LEVODOPA ARE NECESSARY.

DYING NORADRENERGIC NEURONS ARE RELATED TO REM SLEEP DISORDER, A KNOWN RISK FACTOR FOR VH.

A LACK OF ACETYLCHOLINE IS ASSOCIATED WITH VH. CHOLINESTERASE INHIBITORS – SUBSTANCES WHICH PREVENT THE BREAKDOWN OF ACETYLCHOLINE SUCH AS RIVASTIGMINE – ARE ASSOCIATED WITH A DECREASE IN VH.

DEGENERATION OF SEROTONIN RECEPTORS IN ONE PART OF THE BRAIN LEADS TO UPREGULATION IN OTHER PARTS OF THE BRAIN INVOLVED IN VISUAL PERCEPTION. INVERSE AGONISTS OF THESE UPREGULATED RECEPTORS, SUCH AS PIMVANSEMIN, REDUCE VH.

THE N-METHYL-D-ASPARTATE RECEPTOR (ALSO KNOWN AS THE NMDA RECEPTOR), IS A GLUTAMATE RECEPTOR. RILUZOLE, AN ANTIGLUTAMERGIC DRUG WHICH BLOCKS THE NMDA RECEPTOR, DECREASES VH IN CERTAIN PATIENTS.

REDUCED AMOUNTS OF GABA WERE DETECTED IN THE VISUAL CORTEX OF PD PATIENTS WITH VH. BACLOFEN, A GABA AGONIST, CAN TRIGGER VH IN PD.

MELATONIN IS USED TO TREAT REM SLEEP DISORDER. IN A CASE REPORT OF A PWP THE USE OF MELATONIN LED TO REDUCED NOCTURNAL VH.

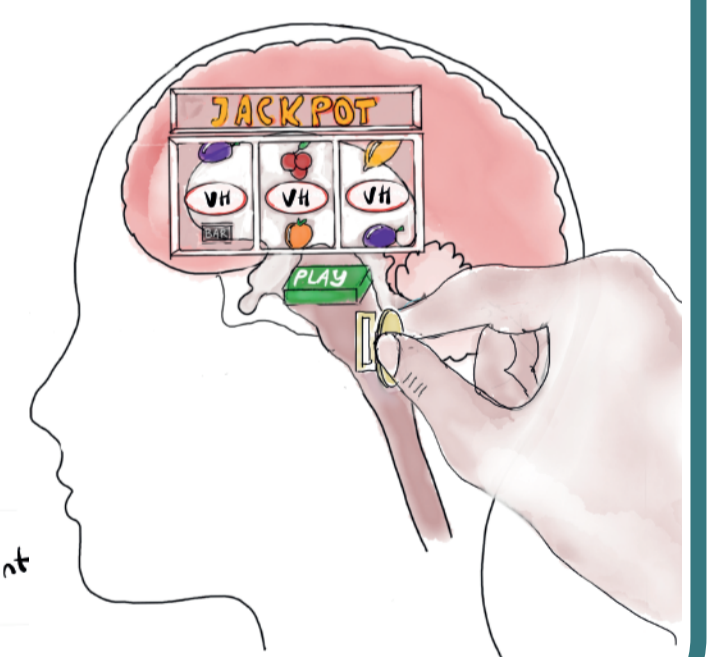
... AND SOME RELATIONS TO VH

To discuss (for patients)

- What are my risk factors?
- How can we manage these?
- Can we review my medication?

RISK FACTORS WHICH INCREASE THE CHANCE OF WINNING THE VH LOTTERY

- older age
- disease severity
- disease duration
- REM sleep behavior disorder
- motor fluctuations
- female sex
- apathy
- depression
- anxiety
- autonomic dysfunction
- visual impairment
- cognitive impairment



TREATMENT

I. PREVENT

INCREASE SOCIAL SUPPORT & EDUCATION

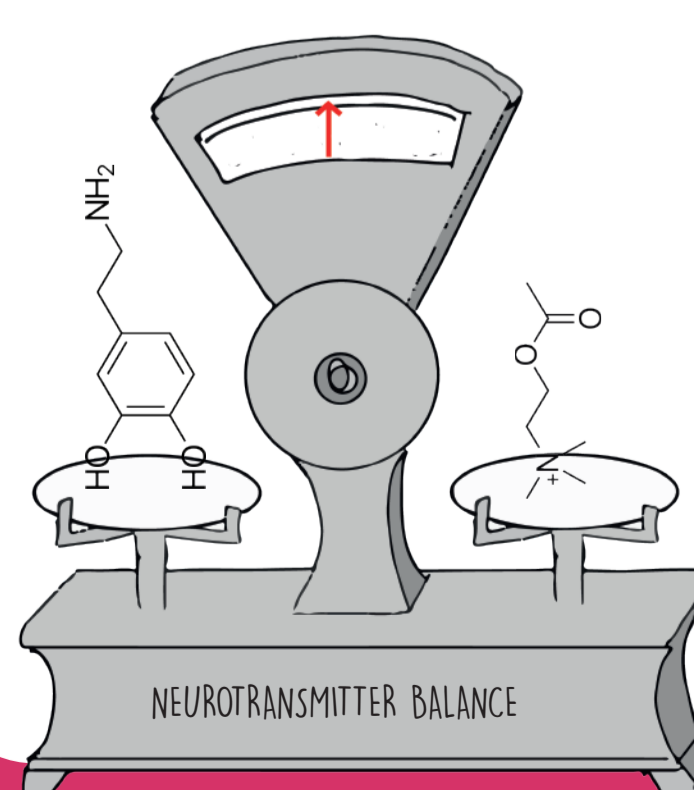
REASSURE PWP THAT THE HALLUCINATIONS AREN'T REAL, E.G. BY APPROACHING THEM TOGETHER.

REDUCE AMBIGUOUS VISUAL INPUT

LITERALLY PUT ON THE LIGHTS TO REDUCE AMBIGUOUS VISUAL INPUT

TACKLE MODIFIABLE RISK FACTORS AND UNDERLYING ILLNESS

E.G. USE AIDS FOR VISUAL IMPAIRMENT AND TREAT MOOD DISORDERS AND LOOK OUT FOR AND TREAT POSSIBLE PROVOKING FACTORS SUCH AS INFECTION, DEHYDRATION, CONSTIPATION ETC.



II. FIND THE RIGHT NEUROTRANSMITTER BALANCE

REVIEW CURRENT MEDICATION

CEASE NONESSENTIAL, POTENTIALLY CONTRIBUTORY MEDICATIONS, PARTICULARLY THOSE MOST RECENTLY ADDED. REDUCE POLYPHARMACY WHEN POSSIBLE.

ADD NEW MEDICATION OR TREATMENTS

CONSIDER CHOLINESTERASE INHIBITORS (WHICH INCREASE THE AMOUNT OF ACETYLCHOLINE) SUCH AS RIVASTIGMINE OR DONEPEZIL

IF VISUAL HALLUCINATIONS PERSIST IN SPITE OF THE ABOVE, CONSIDER ANTISYPHOTOICS OR ELECTRO CONVULSIVE THERAPY