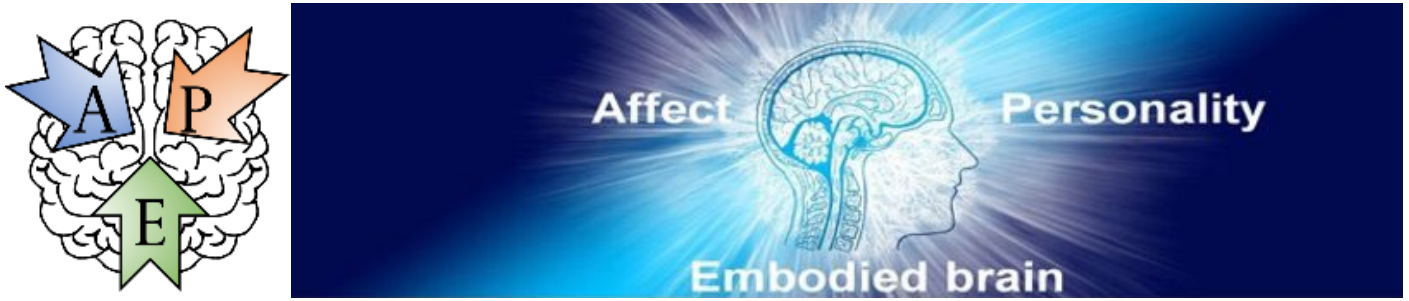




NTU
NOTTINGHAM
TRENT UNIVERSITY

# Psychosis

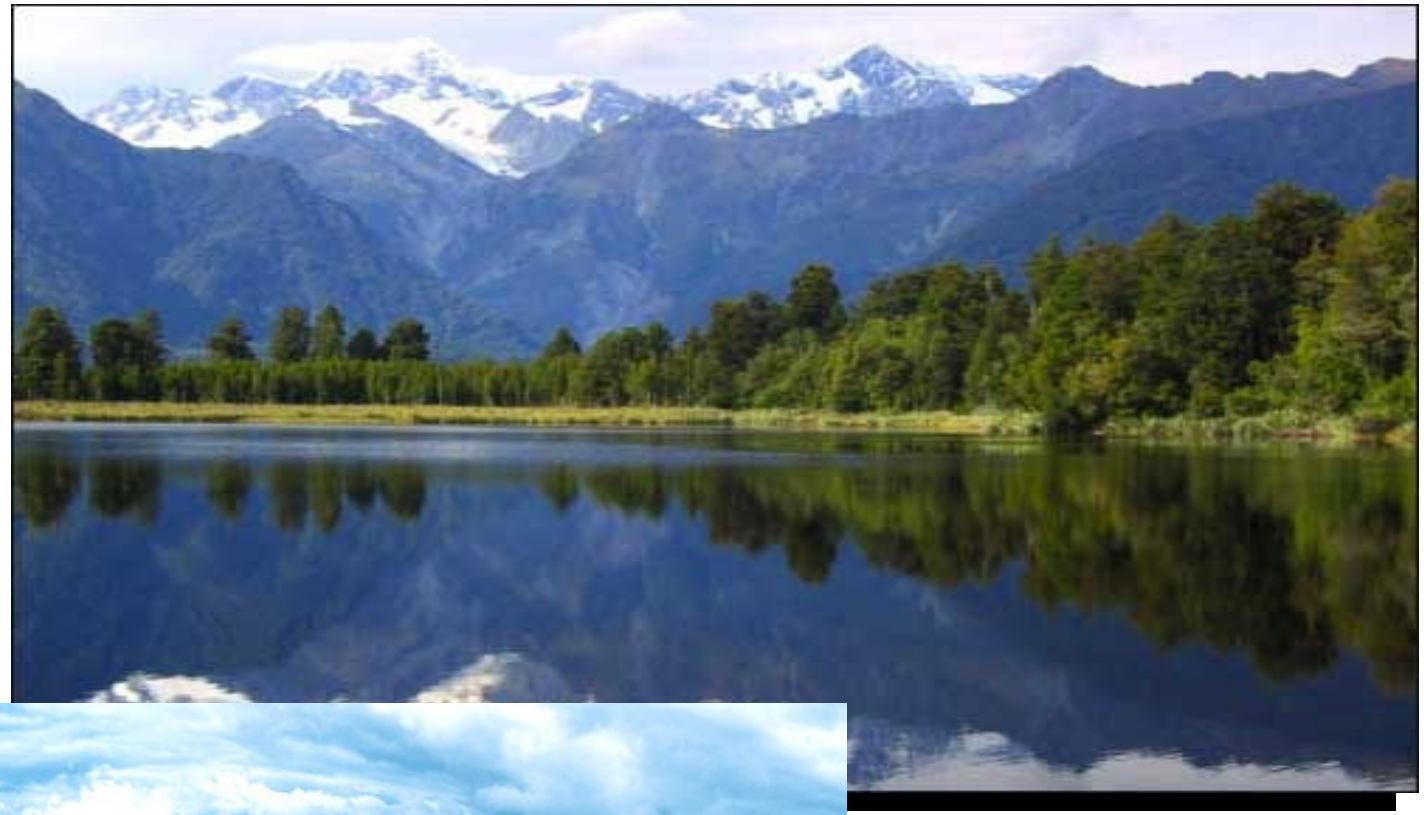
Prof Alex Sumich

Nottingham Trent University (NTU), UK

alexander.sumich@ntu.ac.uk

# Its beautiful!

## ….But holds a dark secret

# Psychosis


- Music
- Art
- Genius
- Inspiration
- Creativity
- Spirituality

**Abnormal condition of the mind/soul**, affecting perception, belief, thinking
**Symptoms:** Hallucinations, Delusions and Thought Disorder

**Healthy vs Unhealthy Psychosis**

**Healthy Psychotic Experiences –** common in childhood (17% prevalence), often transient

**Adult Psychotic Experiences –** awake (8% prevalence), Hypnopompic/Hypnogogic (40%)

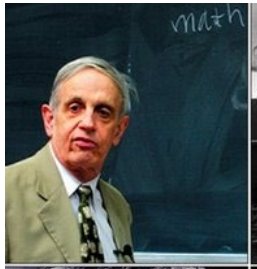
**Subclinical Psychosis** – Personality Traits

**Contribution to Culture** from subclinical/healthy forms of psychosis**: MAGICS**

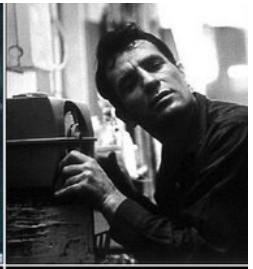
People who hear voices

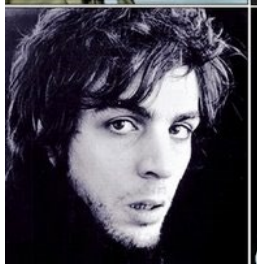
*"During the days when I was living alone in a foreign city … I quite often heard my name suddenly called by an unmistakable and beloved voice. I then noted down the exact moment of the hallucination and made anxious enquiries of those at home about what had happened at that time. Nothing had happened."*

John Nash

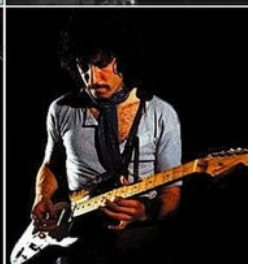



Jack Kerouac





Syd Barrett



Peter Green

Russell Crowe playing Nash in the film *A Beautiful Mind*

# Schizophrenia

**Debilitating, psychotic disorders** (1% general population)

*Clinical Symptoms* – reality distortion, mania, thought disorder, avolition

*Cognitive dysfunction* – attention, memory, executive function, psychomotor speed

Cognitive impairment typically precede, and worsen with clinical onset

**~ Developmental disorder,** despite having an onset in adulthood

**Risk factors for schizophrenia**

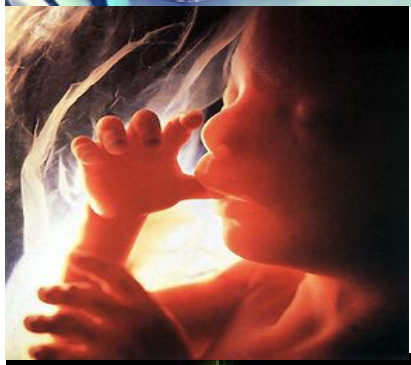
**Hereditary:** monozygotic twins ~50% concordance rates

**Risk Genes:** brain development, brain chemicals (dopamine and glutamate)

**Environmental Component:** Accumulated risk with multiple hits throughout life

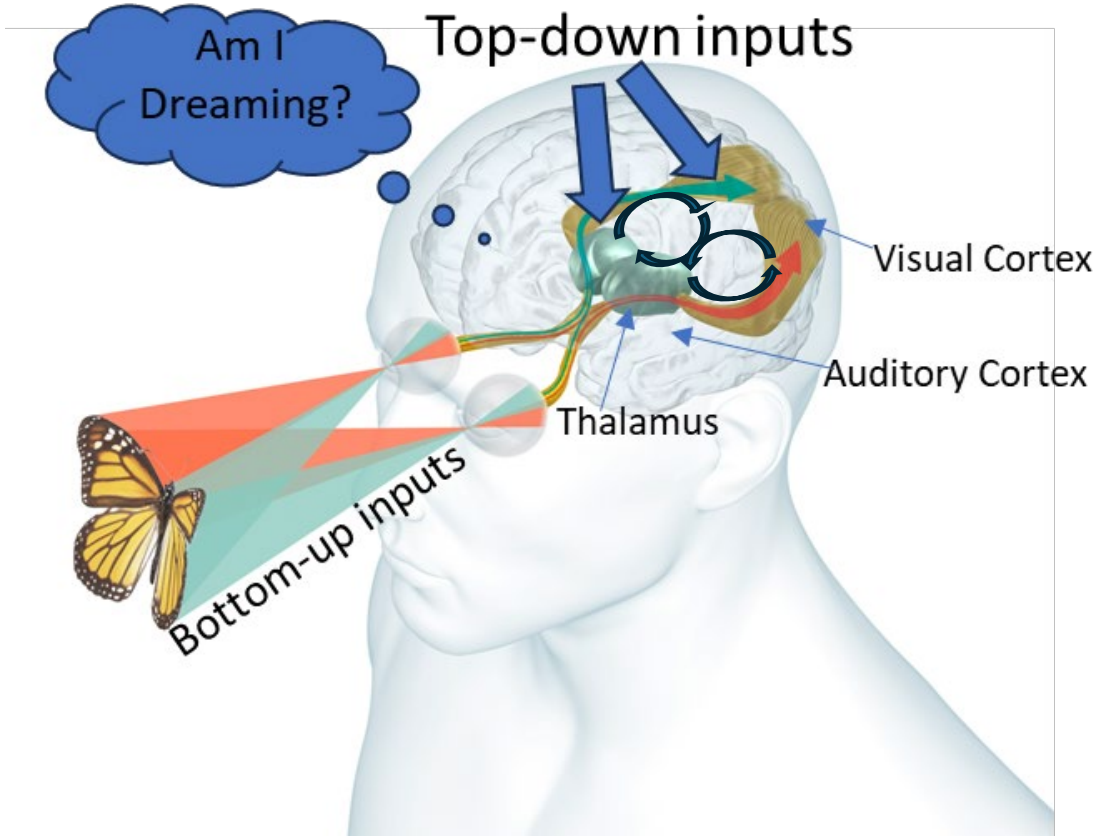
e.g., poor maternal nutrition, trauma, cannabis use, nutrition, adult stress

Risk factors combine, resulting in alteration of typical perception, belief, thinking



# Neurocognitive model of Psychosis

## Typical perception in wake and dreaming





Late last night as the storm blew wild
And I was soundly sleeping
I dreamed a dream, and in that dream
I dreamed that I was dreaming

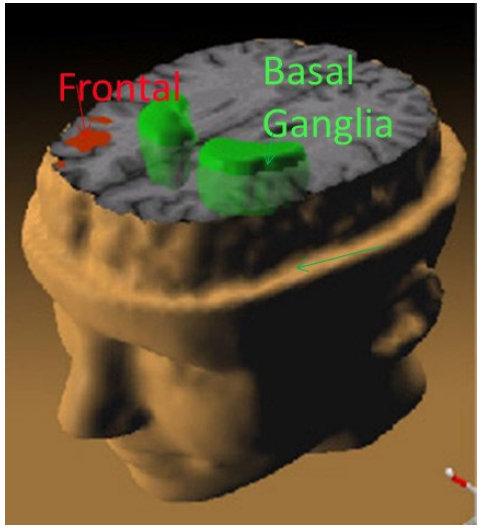
# Prevailing biological theories of schizophrenia

**Dopamine Imbalance Theory:**

Final common pathway for many genetic and environmental risk?

Dopamine excess in *Basal ganglia* – meaning, movement

Dopamine deficiency in *Frontal cortex* – emotions, motivation, monitoring



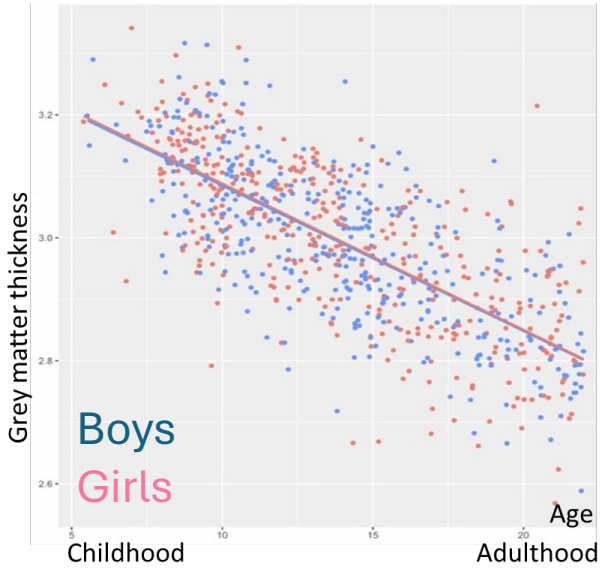

**Dopamine Imbalance**

**Synaptic Pruning Theory**:

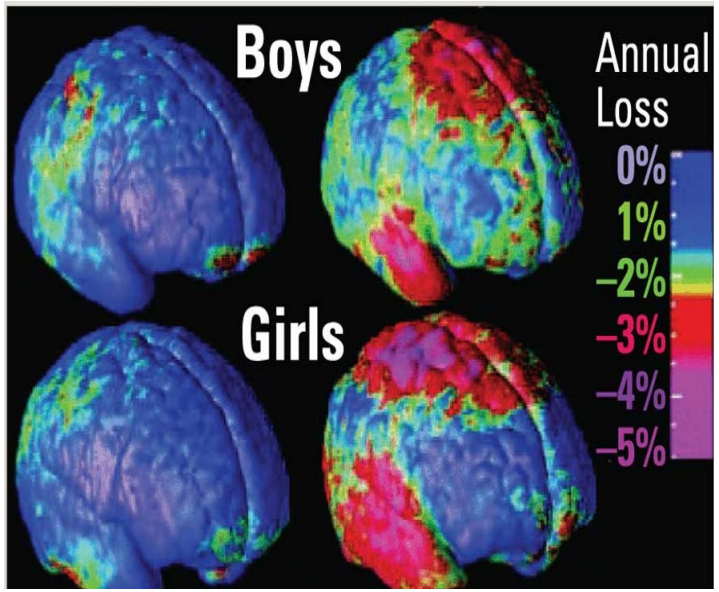
- Brain volume reduction through adolescence
- Improves brain efficiency

**Excessive pruning in schizophrenia**

- Temporal and frontal regions




Controls Schizophrenia




**Synaptic Pruning** (grey matter loss)

# Left Brain: Verbal hallucinations

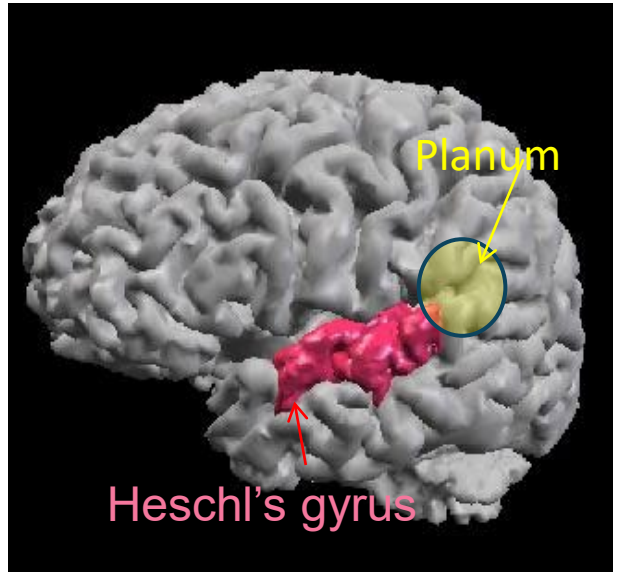
**Superior Temporal Gyrus (STG) in men with recent onset psychosis**

– Anterior STG: Primary auditory cortex (Heschl's)

– Reduced volume of Left Heschl's gyrus ~ severity of **auditory hallucinations** [1, 2]

– Left Posterior STG (planum) ~ disordered language and thought

– Right Posterior STG (planum) ~ social cognition (suspiciousness, paranoia)



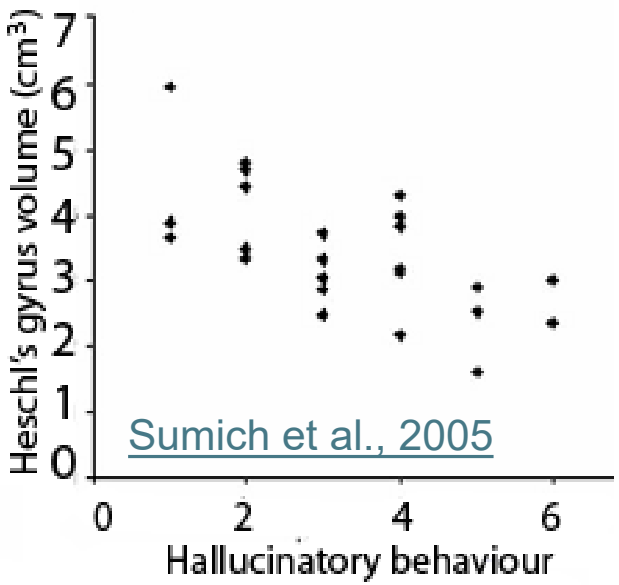

Damage to thalamus (sensory relay)

– impaired glutamate receptor function in thalamus and STG [3]

– Glutamate is the primary activating brain chemical

Hallucinations occur with:

1. **Disrupted bottom-up sensory processing** (STG, Thalamus [3])
2. **Strong top-down input to perception** (excessive basal ganglia dopamine)
3. **Impaired reality monitoring** (deficient medial frontal dopamine)




[1] Sumich et al., (2002) Temporal lobe abnormalities in first-episode psychosis. Am J Psychiatry 159(7):1232-5

[2] Sumich et al (2005) Unreality symptoms and volumetric measures of Heschl's gyrus and planum temporal in first-episode psychosis. Biological Psychiatry, 57(8):947-50

[3] Ettinger et al (2001) Magnetic resonance Imaging of the thalamus in First-episode psychosis. Am J Psychiatry 158(1):116-8

# At risk vs clinical groups

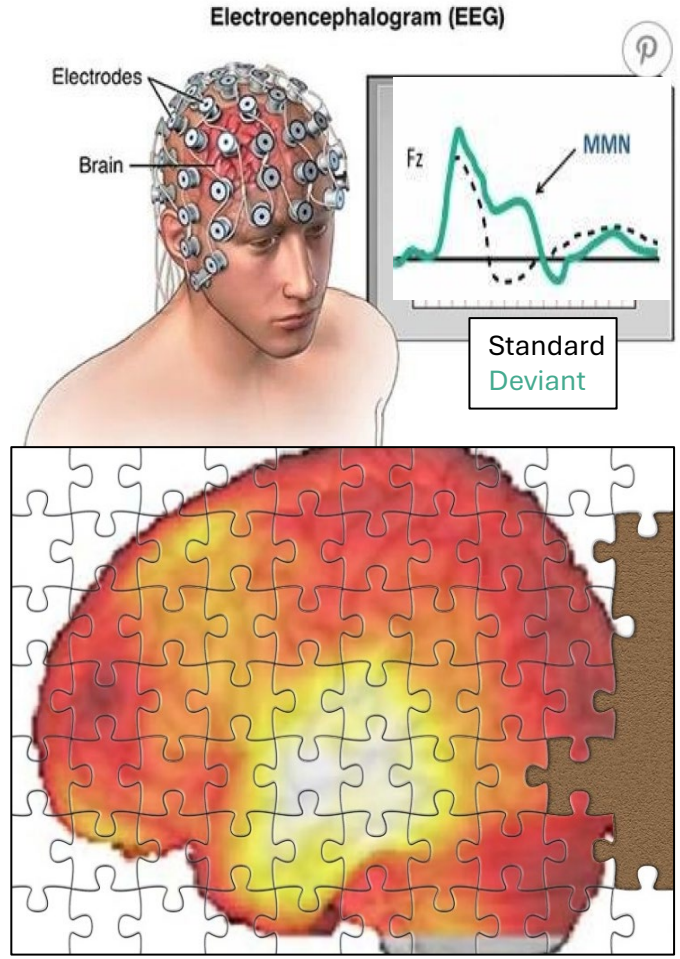
**High-risk groups** (hereditary, subclinical traits) show similar frontal function as people with schizophrenia [4, 5, 6]

**Left temporal deficit is more specific to clinical syndrome (psychosis)**

- Reflected in an EEG measure called Mismatch-Negativity (MMN) [4]
- MMN reflects a preconscious detection of change in physical properties of stimuli
- MMN disruption suggests impaired incoming (bottom-up) information
- Relies on **glutamate** receptors (primary activating brain chemical)

Decline in STG volume (synaptic pruning) coincides with reduced MMN activity

- associated with severity of hallucinations

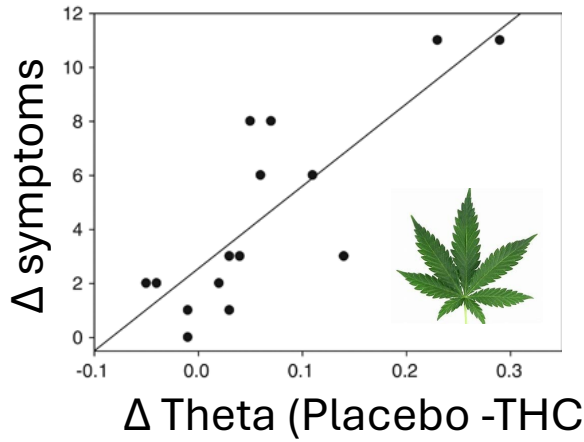



[4] Stone et al., (2010) Thalamic neurochemical abnormalities in individuals with prodromal symptoms of schizophrenia - relationship to auditory event-related potentials. Psychiatry Res. 183(2):174-6.

[5] Sumich et al (2008) Event-related potential correlates of paranormal ideation and unusual experiences. Cortex. 44(10):1342-52.

[6] Sumich et al., (2008) N100 and P300 amplitude to Go and No-Go variants of the auditory oddball in siblings discordant for schizophrenia. Schizophr Res. 98(1-3):265-77.

# Induced psychosis and pseudo-hallucinations




**Intravenous synthetic Δ9-tetrahydrocannabinol (THC)**

- Disrupts communication between left and right frontal regions
- Reduction in frontal communication parallels severity of induced psychosis [7,8]

**Ganzfeld Paradigm**

- Bottom-up information is degraded using white-out mask
- Top-down mechanisms struggle to make sense of input
- Induces pseudo-hallucinations [9,10]
- Greater propensity to hallucinate ~ reduced EEG (alpha) activity in visual sensory areas
    - NTU Psychology's first virtual reality headset

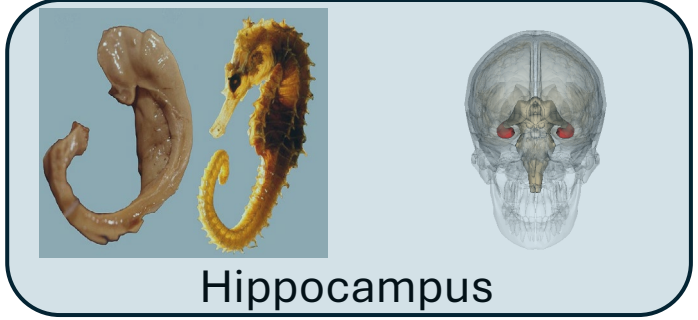
[7] Morrison et al., (2011). Disruption of frontal θ coherence by Δ9-tetrahydrocannabinol is associated with positive psychotic symptoms. Neuropsychopharmacology. 36(4):827-36. .

[8] Stone et al., (2012) Communication breakdown: delta-9 tetrahydrocannabinol effects on pre-speech neural coherence. Mol Psychiatry. 17(6):568-9.

[9] Sumich et al., (2018) Reduction in lower-alpha power during Ganzfeld flicker stimulation is associated with the production of imagery and trait positive schizotypy. Neuropsychologia. 121:79-87

[10] Zandbagleh (2023) et al., Graph-based analysis of EEG for schizotypy classification applying flicker Ganzfeld stimulation. Schizophrenia (Heidelb). 9(1):64.

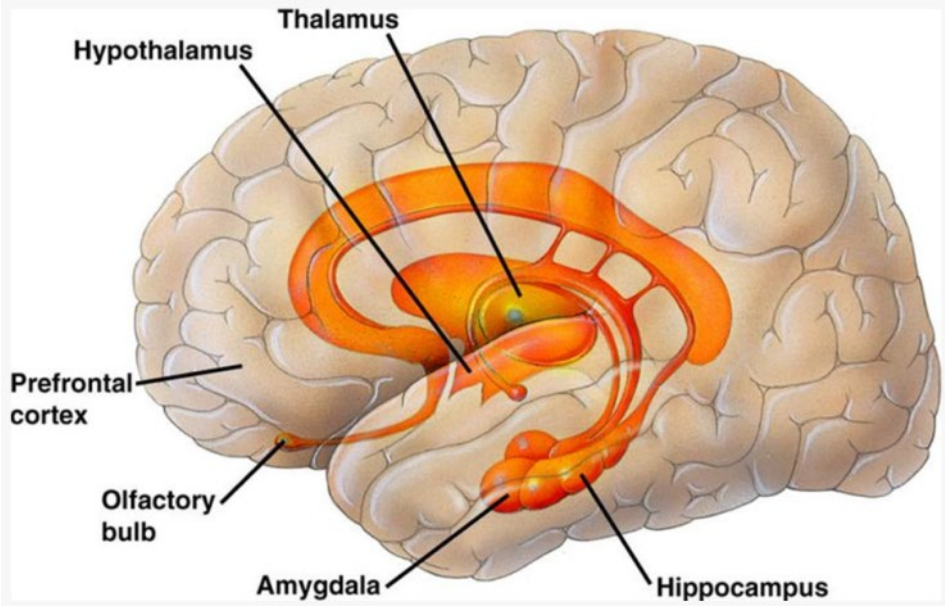
# Memory and Emotions affect Perceptions




**Dysregulation of threat response, negative internal dialogue and poor social cognition exacerbate persecutory delusions** [11, 12, 13]

**Amygdala and Hypothalamus**
– experience of negative affect (e.g., fear, sadness, anxiety)

Hyperactivation of amygdala and hypothalamus
– hyperdopaminergia and hypo-serotonergia
– Poor frontal, hippocampal and thalamic function [3, 13] - **Impaired emotional regulation**
– hypersensitive threat response (even to neutral stimuli)
– Impact of trauma of self-schema




11. Pinkham AE, Liu P, Lu H, Kriegsman M, Simpson C, Tamminga C. (2015) Amygdala Hyperactivity at Rest in Paranoid Individuals With Schizophrenia. Am J Psychiatry. 172(8):784-92.
12. Freeman D. Suspicious minds: the psychology of persecutory delusions. Clin Psychol Rev. 2007 May;27(4):425-57.
13. Salvatore G, Lysaker PH, Popolo R, Procacci M, Carcione A, Dimaggio G. (2012) Vulnerable self, poor understanding of others' minds, threat anticipation and cognitive biases as triggers for delusional experience in schizophrenia: a theoretical model. Clin Psychol Psychother. 19(3):247-59.
14. Sumich A, Chitnis XA, Fannon DG, O'Ceallaigh S, Doku VC, Falrowicz A, Marshall N, Matthew VM, Potter M, Sharma T. (2002) Temporal lobe abnormalities in first-episode psychosis. Am J Psychiatry. 159(7):1232-
3. Ettinger et al (2001) Magnetic resonance Imaging of the thalamus in First-episode psychosis. Am J Psychiatry 158(1):116-8

# Beyond the brain

Immune and Enteric systems affect functional connectivity [15]

**Immune system** – defence against infection, activating inflammatory response

– Chronically raised **inflammation** exacerbates non-communicable diseases

– Activated with psychological pain: stress/negative affect

– Raised inflammation alters brain function, increasing vulnerability to *rigid, negative emotions* [16. 17]

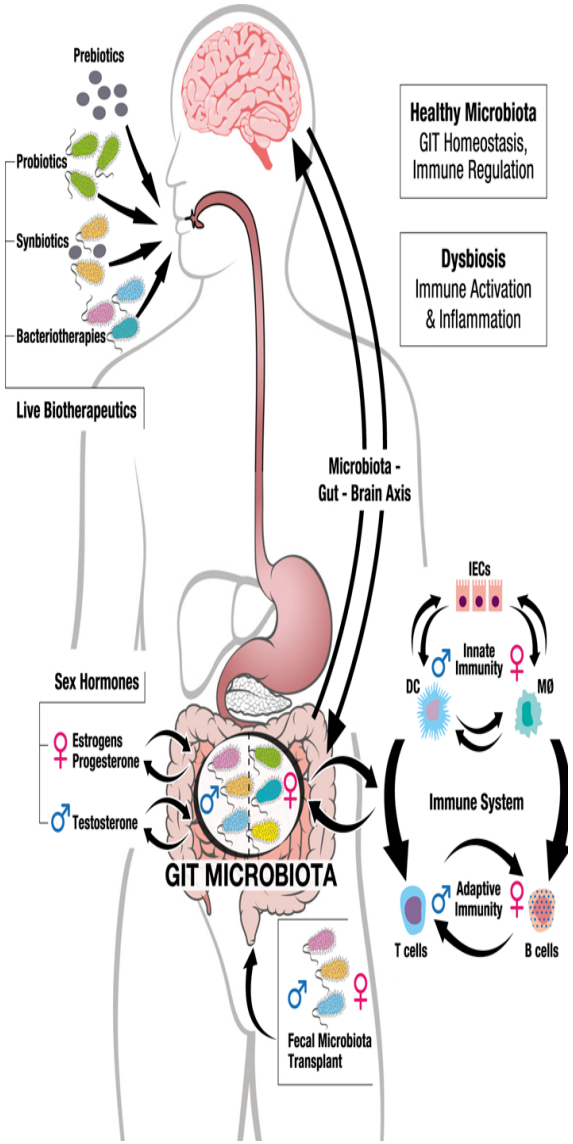
**Enteric system – gut microbiome** [16. 17]

Communication with brain, affecting how we think and feel [17]

– Direct path – Vagal Nerve

– Indirect path – Inflammation, Hormone release (e.g., cortisol), production of fatty acids

**Nutrition** affects the immune system and gut function [18]





15. Doborjeh et al., (2025) Neurocomputational Modelling of EEG Connectivity: Links Between Depression, Inflammation, and Gut-Microbiome, conference proceedings

16. Heym et al,. (2019) The role of microbiota and inflammation in self-judgement and empathy: implications for understanding the brain-gut-microbiome axis in depression. Psychopharmacology (Berl) 236, 1459–1470

17. Sumich et al., (2021) Gut microbiome-brain axis and inflammation in temperament, personality and psychopathology. Current Opinion in Behavioral Sciences, 44, 101101

18. Lenzoni et al., (2025) Investigating the relationship between gut microbiota and electrocortical signatures of feedback processing: an ERP study. Psychopharmacology (revised submission)

# Tryptophan Catabolism

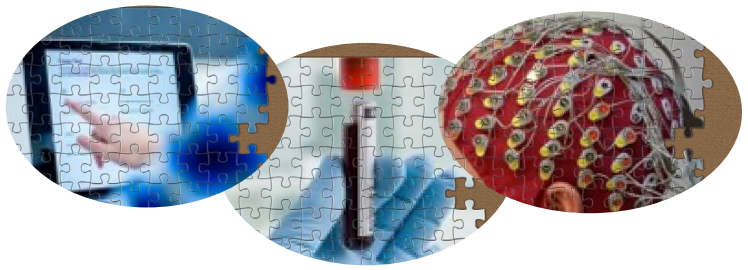
BIAL Foundation

**Tryptophan –** amino acid, found in many foods
- precursor to serotonin

Inflammation activates **tryptophan catabolism**
- deficient serotonin

**Bifurcating pathways: Kynurenine metabolites**
- Kynurenic Acid (Excessive in Schizophrenia)
- Quinolinic Acid (Excessive in Depression)

**BioTAP Study:** Effect of trauma on wellbeing



**Kynurenine pathways**

INFLAMATION

**Tryptophan** → **Serotonin**

L-Kynurenine →

**Kynurenic Acid**
Protects against damage
Blocks glutamate
Dysregulates dopamine
Increases synaptic pruning (?)
High in Schizophrenia
Low in Major Depression
Low in Dementia

**Quinolinic Acid** (neurotoxic)
Activates Glutamate (NMDA) receptors
Hypersensitive amygdala – intense negative affect
High in Major Depression (and dementia)

# Genetic risk for psychosis

**Machine learning:** applied to socio-cognitive and genetic data [19, 20, 21, 22]

**Longitudinal Youth-at-Risk Study (LYRIKS):** Individuals at ultra high-risk for psychosis – assessed 6-monthly, across 24 months

**Identify genes relevant to maintenance of risk state:**
- Neuroinflammation and brain development (TSPAN2) [20, 21]
- Kynurenic acid production (transamination; GOT2) [22]
- Gut function (fatty acid binding proteins) [22]

The other NTU


19 Doborjeh et al., (2023) Investigation of social and cognitive predictors in non-transition ultra-high-risk' individuals for psychosis using spiking neural networks. Schizophrenia, 9(1), 10.
20 Tan (2023) RNA-sequencing of peripheral whole blood of individuals at ultra-high-risk for psychosis - A longitudinal perspective. Asian J Psychiatry, 89, 103796.
21 Singh et al., (2023) Constrained neuro fuzzy inference methodology for explainable personalised modelling with applications on gene expression data. Sci Rep., 13(1), 456.
22 Doborjeh et al., (in Prep) Genetic Predictors of Social and Cognitive Functions in Ultra-High-Risk Individuals for Psychosis

# Psychological Interventions:

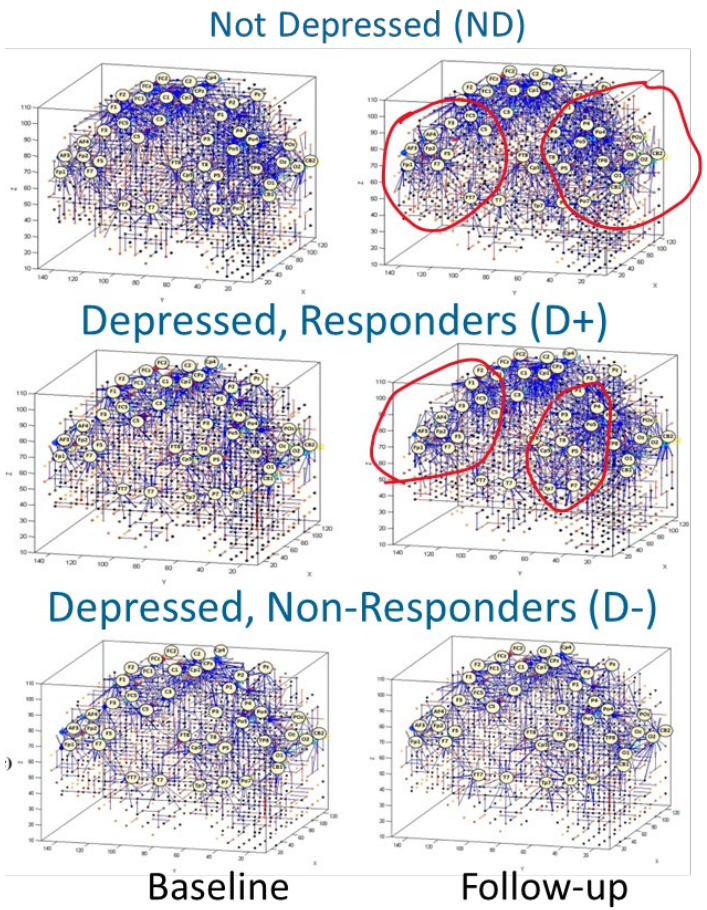
**Self-compassion – kindness, non-judgmental:** makes hallucinations nicer

**Mindfulness**: "the awareness that arises from paying attention on purpose, in the present moment, and non-judgmentally (Kabat-Zinn, 2005)"

**Mindfulness Training improves wellbeing** (lowers depression, anxiety) [23, 24]
**Alters brain function**: raises frontal and temporal connectivity [25]

- greater increase in connectivity in responders

**Predicting response**:
Based on baseline EEG, Machine learning methods – 87% accuracy[25, 26]





23 Van Gordon et al. (2014). Meditation Awareness Training (MAT) for Psychological Well-Being in a Sub-Clinical Sample of University Students: A Controlled Pilot Study, Mindfulness, 5, 381–391
24. Krägeloh et al. (2019). A pilot randomized controlled trial for a videoconference-delivered mindfulness-based group intervention in a nonclinical setting. Mindfulness, 10, 700–711.
25. Doborjeh et al. (2019). Spiking Neural Network Modelling Approach Reveals How Mindfulness Training Rewires the Brain, Scientific Reports, 9, 6367
26. Doborjeh et al. (2020). Interpretability of Spatiotemporal Dynamics of the Brain Processes Followed by Mindfulness Intervention in a Brain-Inspired Spiking Neural Network Architecture. Sensors, 20(24), 7354

# Havening for trauma recovery

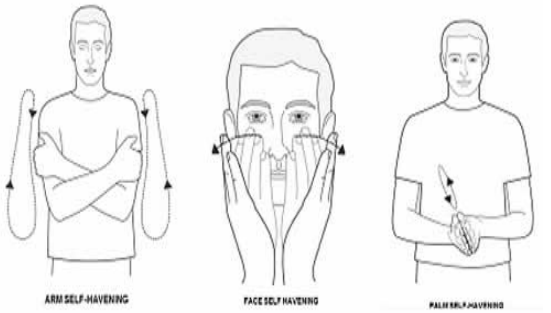
HAVENING TECHNIQUES®

**Havening:** [27, 28]
- Harnesses the power of nurturing touch
- to reduce trauma, foster affirmation

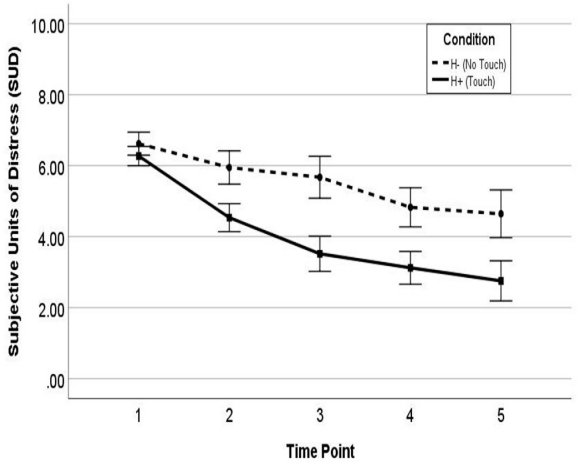
**Nurturing Touch** – vital for life and wellbeing
- stimulates oxytocin release

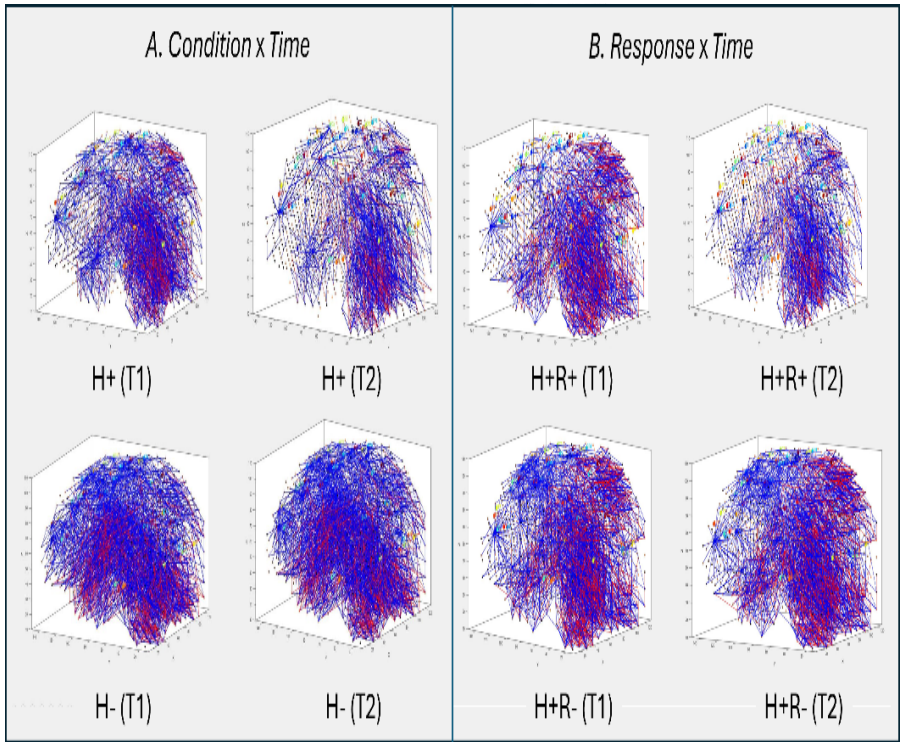
**Oxytocin** (Huggytocin; RTM®) hormone
- released during affiliative social contact
- regulates stress & immune response
- makes amygdala more efficient

**NTU Havening study**
- Havening Touch reduces subjective distress [27]
- calms anterior temporal cortex [28]




Self-Havening




27. Sumich et al., (2022) The power of touch: The effects of havening touch on subjective distress, mood, brain function, and psychological health. Psychology & Neuroscience, 15(4), 332–346
28. Sumich et al., (2024) Calming the mind: Spiking neural networks reveal how Havening Touch to reduce persistent distress attenuates left temporal electroencephalographic connectivity. Conference proceedings ICONIP, 2024

*"For me the Voice of God, of Conscience, of Truth, or the Inner Voice or 'the Still Small Voice' mean one and the same thing. I saw no form. I have never tried, for I have always believed God to be without form. But what I did hear was like a Voice from afar and yet quite near. It was as unmistakable as some human voice definitely speaking to me, and irresistible. I was not dreaming at the time I heard the Voice. The hearing of the Voice was preceded by a terrific struggle within me. Suddenly the Voice came upon me. I listened, made certain it was the Voice, and the struggle ceased. I was calm. The determination was made accordingly, the date and the hour of the fast were fixed…"*

*"Initially I did not hear any voices. Some years went by before I heard voices and — I became first disturbed in 1959, and I didn't hear voices until the summer of 1964 I think, but then after that, I heard voices, and then I began arguing with the concept of the voices. And ultimately I began rejecting them and deciding not to listen, and, of course, my son has been hearing voices, and if he can progress to the state of rejecting them, he can maybe come out of his mental illness."*

???? started to hear voices when she was 13. She believed these voices were angels and saints, messengers from God. Whilst ???? was initially scared of the voices, and felt unable to talk to others about them, she began to build a better relationship with them. Some of these angels appeared in visions, as faces or – sometimes – accompanied by bright light.