

UK Neuropsychiatry Landscape

Tremendous advances in the science and clear opportunities for UK leadership

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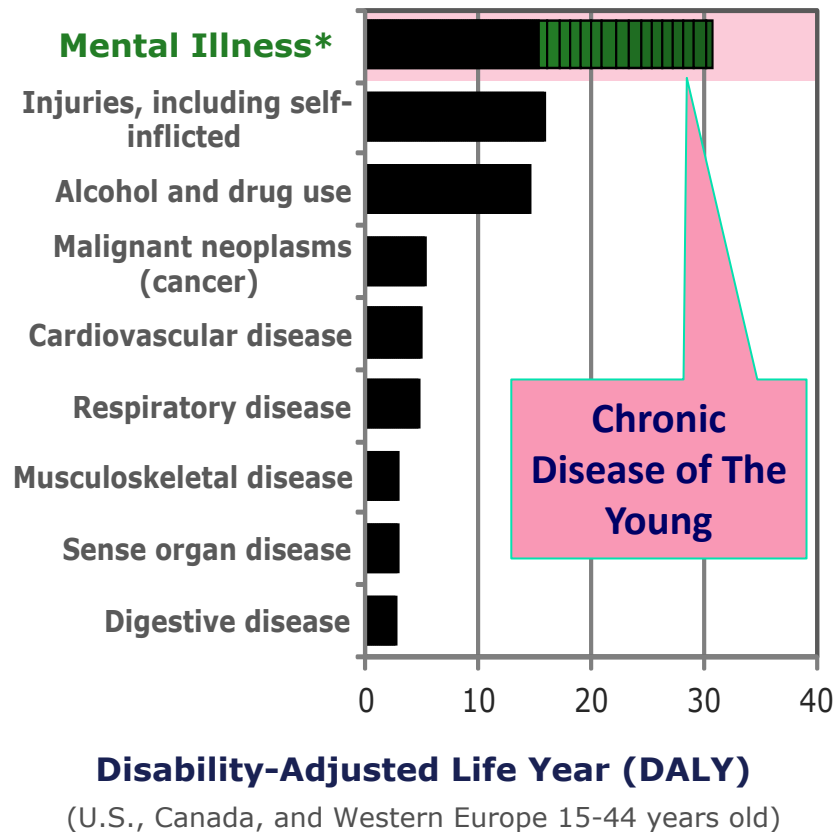
Previously: Head of Global Neuroscience R&D, Janssen/J&J

Previously: Director, NIMH Mood and Anxiety Disorders Program

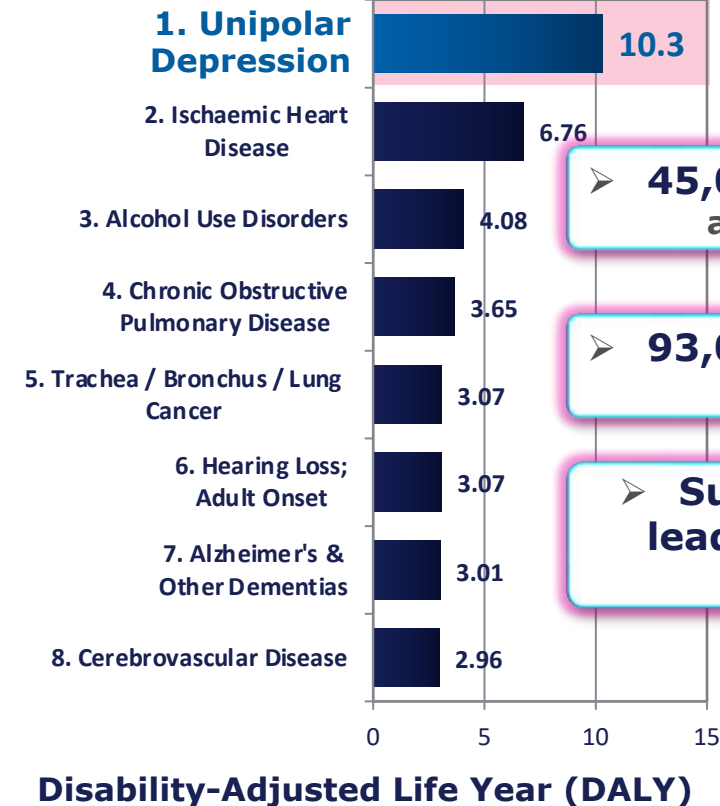


Serious Mental Illnesses are Major Causes of Disability Worldwide: Global Burden of Disease

Leading Disease Categories (DALY)



Leading Individual Disease (DALY)



➤ **45,000** deaths by suicide annually in the USA

➤ **93,000** deaths by suicide annually in the EU

➤ **Suicide now the 2nd leading cause of death in girls 15-19**

2011 World Economic Forum report

mental illnesses globally will cost more than cancer, diabetes, & chronic respiratory diseases combined!

Tremendous Impact on Physical Health too

Major Impact on Physical Health too / Prevalence

SYSTEMIC

↑ MIGRAINES, ↑ THYROID DISEASE

HPA Axis Dysregulation

↓ ACTH, ↑ CORTISOL ↔ GH

Innate Immune System

INFLAMMATORY CYTOKINES:

(↑ IFN- γ , ↑ IL-1, ↑ IL-6, ↑ TNF- α)
↑ TRAIL (TNF SUPERFAMILY) ↔ FATIGUE SYNDROME

ALTERATION OF KYNURENINE PATHWAY:

↑ IDO ↔ ↑ MICROGLIAL ACTIVATION ↔ ↑ QA OR ↑ QA/KYNA RATIO ↔ NEUROTOXICITY;
↓ ASTROCYTE FUNCTION ↔ ↓ KYN, KYNA ↔ ↑ GLU SPILLOVER.

Cardiovascular Risk:

↑ MI RISK OF DEATH BY 3.5, ↓ HRV,
↓ VEGF, ↑ RISK FOR DIABETES

GI System and Adipose:

↑ BMI (CENTRAL & VISCERAL ADIPOSITY);
↑ ↓ ADIPOKINES (↓ ADIPONETINS, ↑ RESISTIN, ↓ LEPTIN, GREHLIN AND ↑ ↓ MICROBIOME)

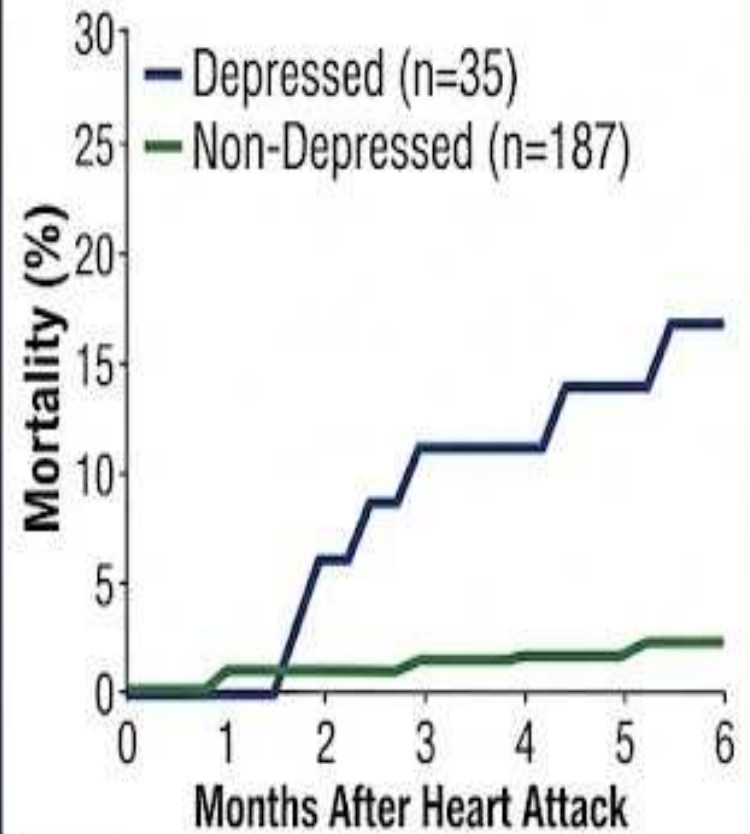
Osteoporosis:

↑ STOROTED SCORE, RANKL ↑ ↓ RANKL



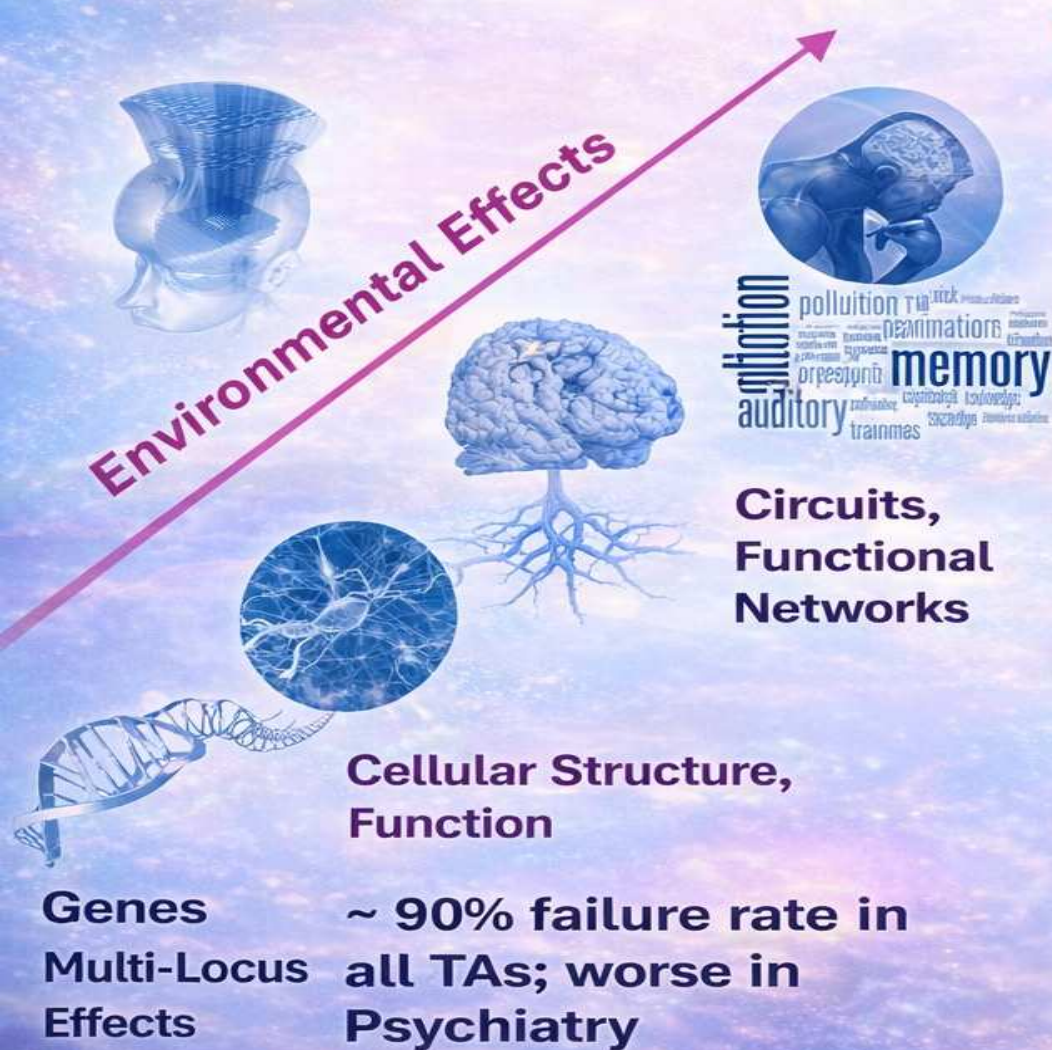
Kadriu et al 2017 *Mol Psych*
Not simply lifestyle - shared biology too

Outcomes: Cumulative Mortality for Depressed & Non-depressed Patients Following MI



Frasure-Smith et al

Biopharma has returned to neuropsychiatry because the science has advanced tremendously



Optogenetics in the Mouse CNS

Cell-type specific control of neural activity with light

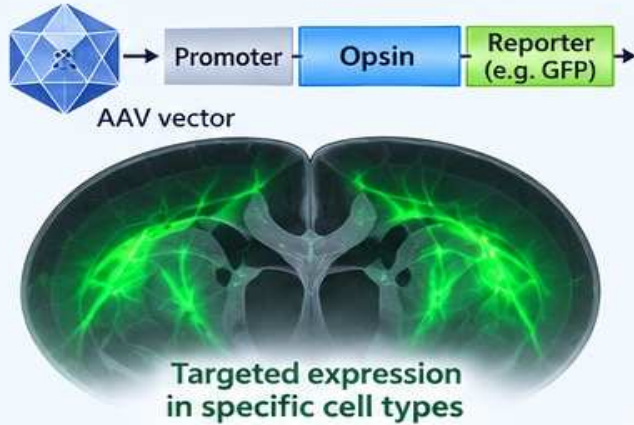


Nobel Prize in Physiology or Medicine 2026

Awarded for the development of optogenetics and its transformative impact on neuroscience.

1 Genetic targeting of light-sensitive proteins

Viral vectors or transgenic mice drive expression of opsins in defined neurons using cell-type specific promoters (e.g., CaMKII, PV, DAT).

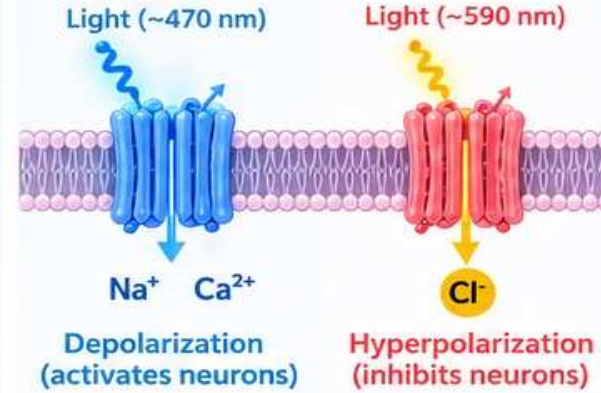


2 Opsin expression in neurons

Example opsins:

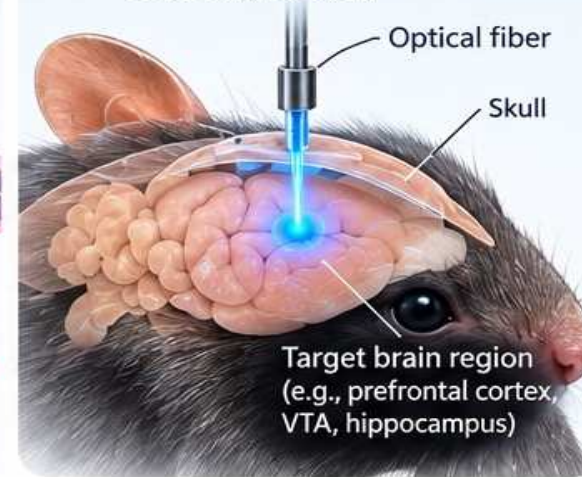
Channelrhodopsin-2 (ChR2)

Halorhodopsin (NpHR) or ArchT



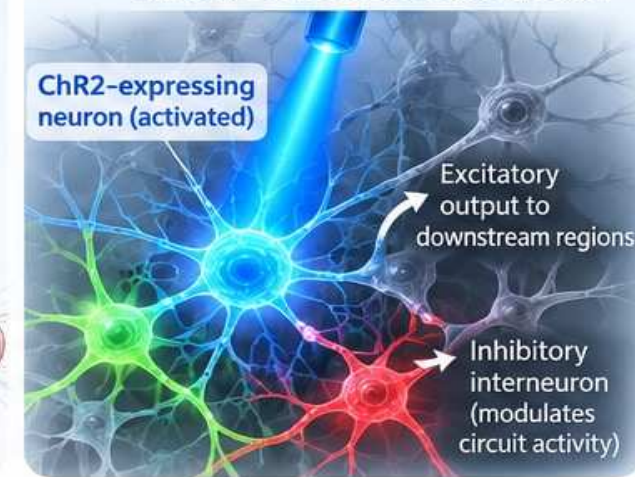
3 Light delivery to the brain

An optical fiber or implanted LED delivers precise flashes of light to the target region.

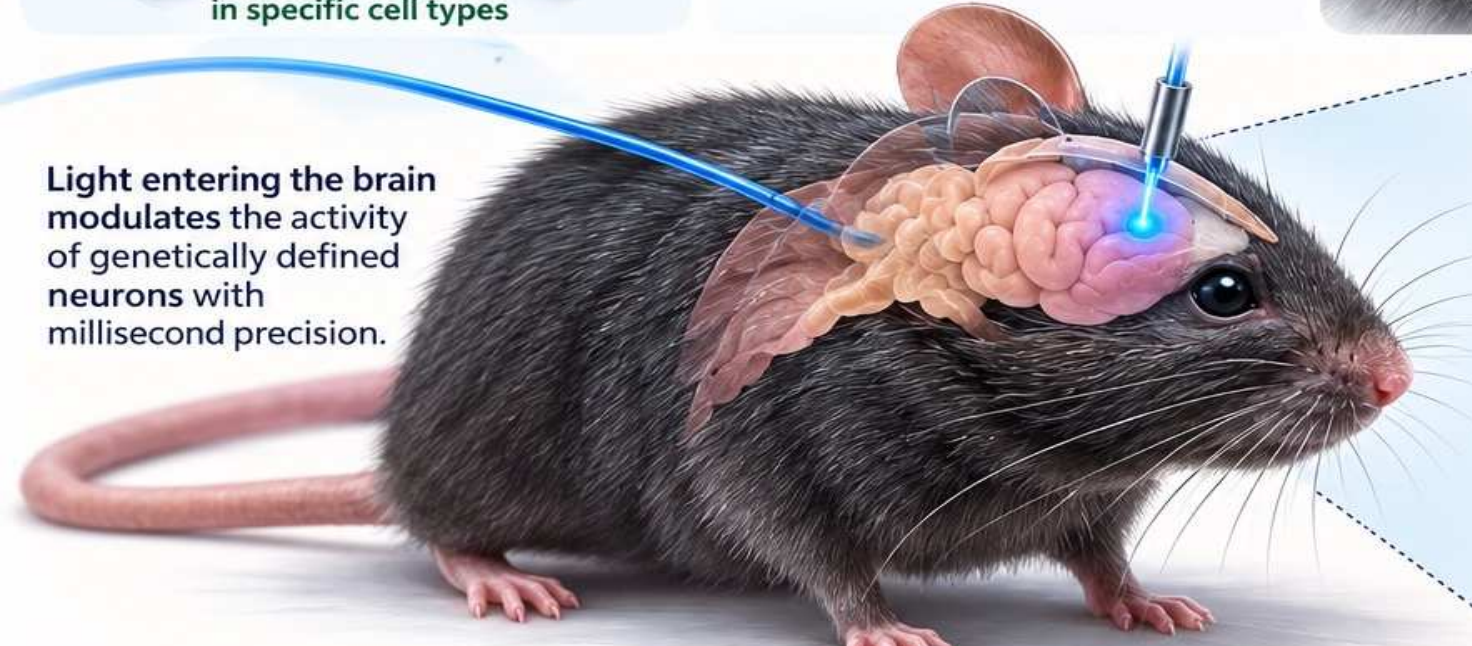
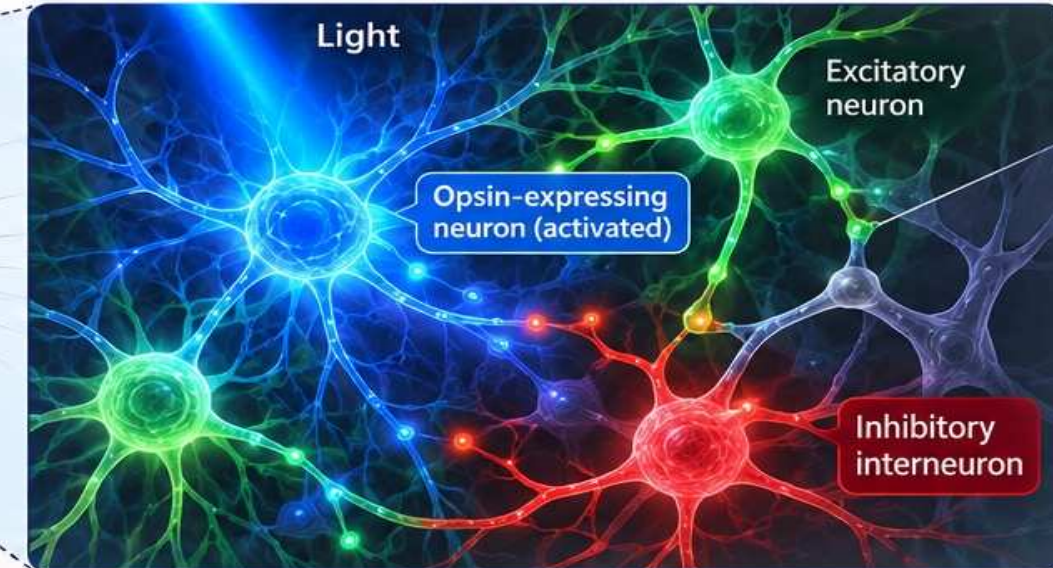


4 Cell-type specific control in neural circuits

Light selectively activates or inhibits the targeted neurons within circuits.



Light entering the brain modulates the activity of genetically defined neurons with millisecond precision.



Beyond Visualizing Neural Plasticity:

In Vivo Manipulation at the Cell & Circuit Level



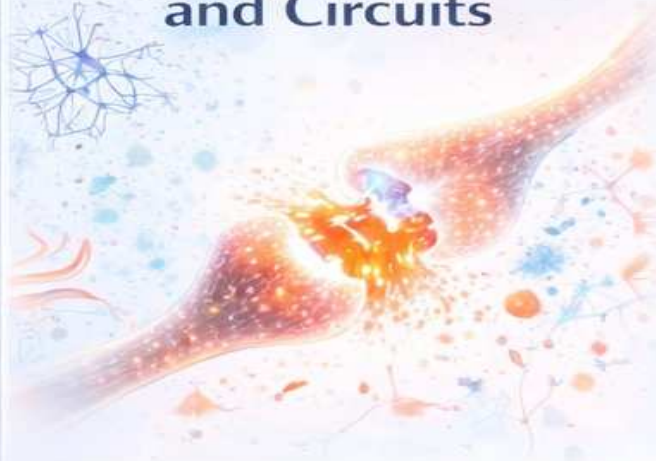
Deisseroth, Stanford

Very exciting novel, improved targets have emerged for Ψ :
need to identify patient sub-groups most likely to respond to each

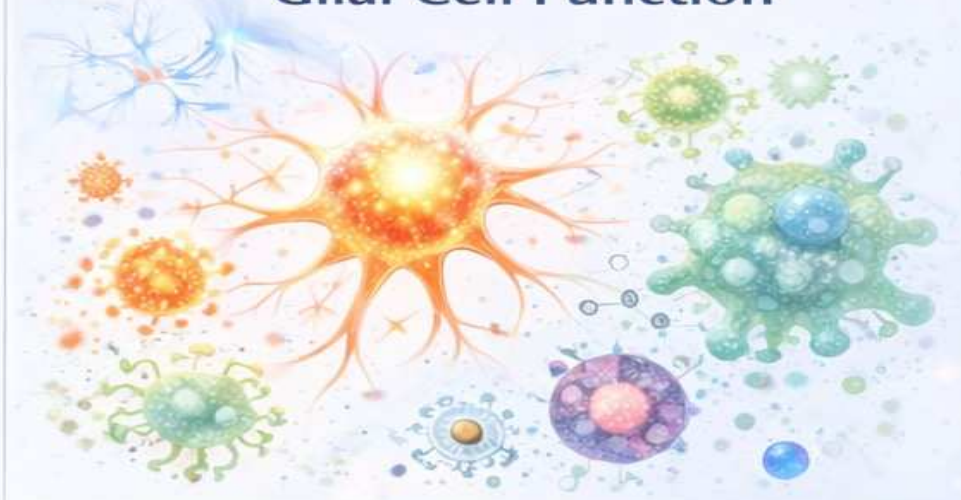
Genetic/Epigenetic Targets



**Synaptic Plasticity
and Circuits**



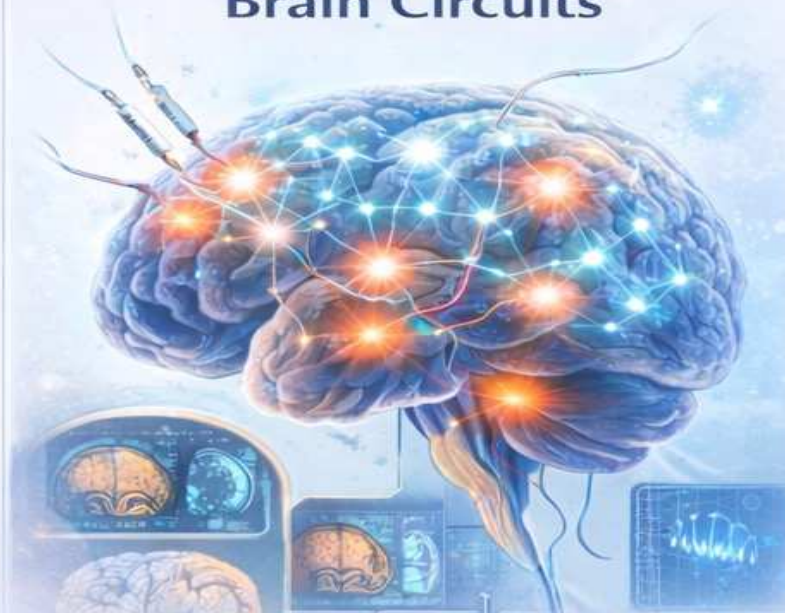
Glial Cell Function



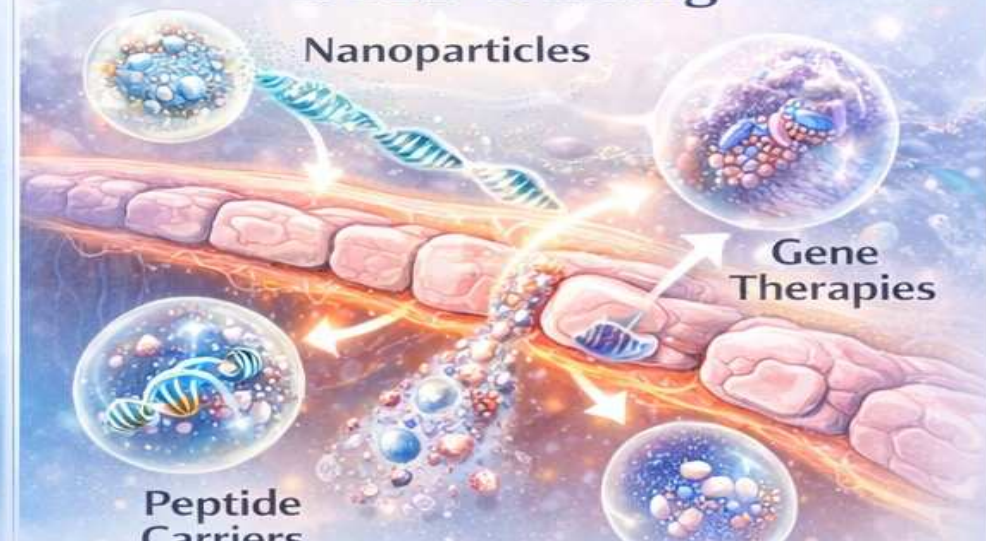
Neuroinflammation



Brain Circuits



**Protein/Nucleotide Rx's
& BBB Crossing**



MDD is associated with elevations of selected cytokines: mediate depression in sub-populations?



SYSTEMIC

↑ MIGRAINES, THYROID DISEASE

HPA AXIS

↑ GH ↑ Cortisol, ⇌ ↓ GH

INFL

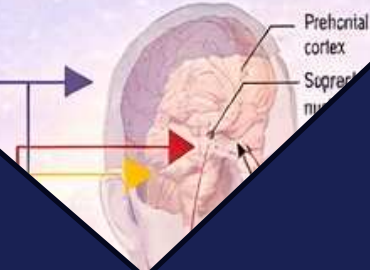
CARDIOVASC

↑ MI, Heart

↑ Stroke, ↑

GI SYSTEM AND ADIPOSE:

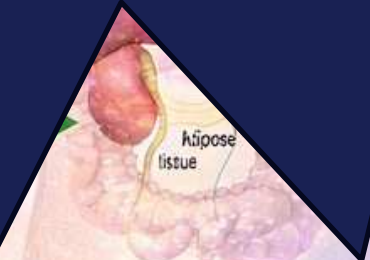
↑ BMI (VISCERAL & VISCERAL ADIPOSIT),
↑ ↑ INSULIN RESISTANCE ↑ DECREASED GLUT-4
↑ GIP C (↓ LEAN OPTIN (↑ OBESITY, CVAD & NON-R.



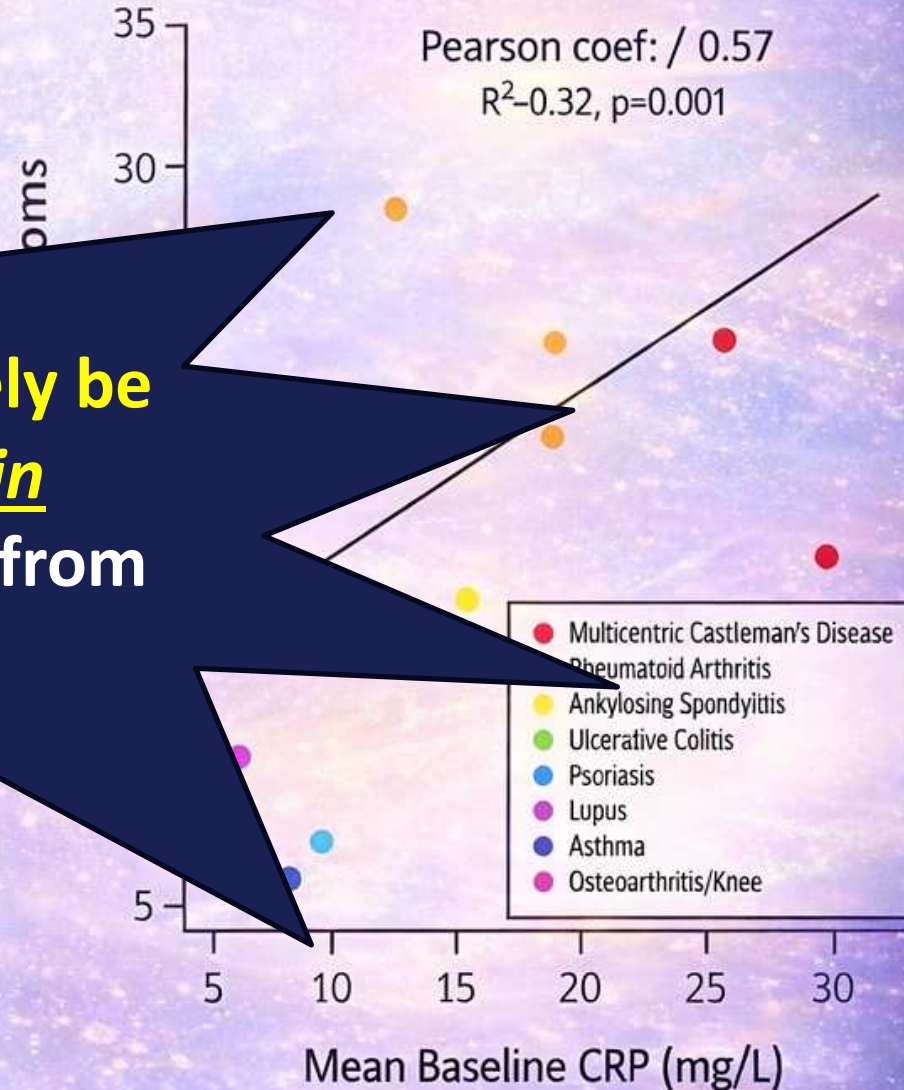
Prehioral cortex

Supra

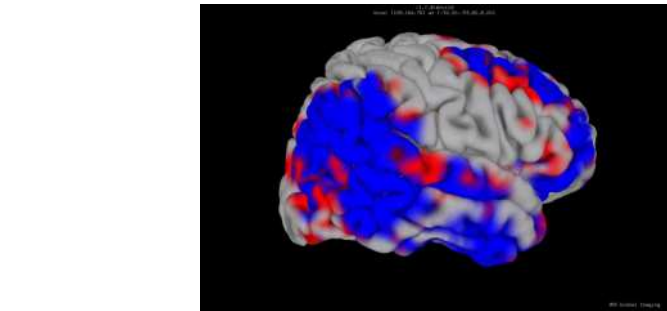
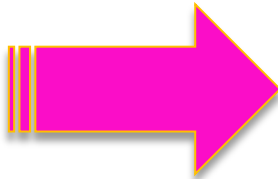
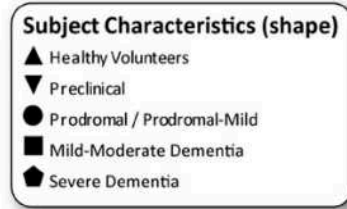
pituitary



Adipose tissue



Immune-based Rx's will likely be
very beneficial for certain
patient subtypes: get away from
“one size fits all”



AI to Decode Complex Neuropsychiatric Disorders and Enable Precision Psychiatry

NEUROPSYCHIATRIC DISORDERS ARE COMPLEX

Many interacting factors across multiple levels



Genes



Brain structure and function



Neurotransmitters and immune factors



Clinical history and symptoms



Environment and lifestyle



Digital and real-world data

AI FINDS HIDDEN PATTERNS

Integrating diverse data to understand biological subtypes and predict outcomes

AI

ENABLING PRECISION PSYCHIATRY

The right treatment, for the right person, at the right time



More accurate diagnosis



Targeted treatments



Better outcomes



Fewer side effects



From complexity
across many levels



To deeper understanding
powered by AI



To personalized care
and brighter futures

PILLAR 1: ACADEMIC EXCELLENCE & RESEARCH POWER



UNIVERSITY OF
OXFORD

KING'S
College
LONDON



UNIVERSITY & CAMBRIDGE

UCL

- World-Leading Universities & Institutes (University of Oxford, UCL, University of Cambridge, NIHR, MRC, BRCs)
- High-Impact Publications
- Global Neuro Research Leader

PILLAR 2: INTEGRATED NHS INFRASTRUCTURE

NHS



- Centralized Patient Records (NHS Digital)
- Diverse Patient Populations (Dementia, Depression, Schizophrenia)
- CRFs & Dedicated Networks
*OFH: [Test description, e.g., Our Future Health]

PILLAR 3: ADVANCED BIOMARKERS & PHENOTYPING



- State-of-the-Art Imaging & Neurophysiology
- Fluid & Genetic Biomarkers (Biobanks, Genomics)
- Deep Phenotyping & Cognitive Assessment Tools

UK's LEADING STRENGTHS IN NEUROPSYCHIATRY TRIALS

Translational • Proof-of-Concept • Phase 2



PILLAR 4: REGULATORY & OPERATIONAL EFFICIENCY



- Efficient Framework (MHRA)
- HRA & Ethics Approvals
- Fast-Track Schemes (ILAP) & Novel Designs

PILLAR 5: VIBRANT ECOSYSTEM & PARTNERSHIPS



- Thriving Life Sciences (Pharma, Biotech)
- Strong Academic-Industry Collabs
- Investment & Funding
- CRN Access

Mood Disorders Network

Treatment-resistant and
difficult-to-treat depression



15 NHS-embedded research clinics

— delivering experimental medicine, early-phase studies and commercial trials at scale

Standardised data across every site.

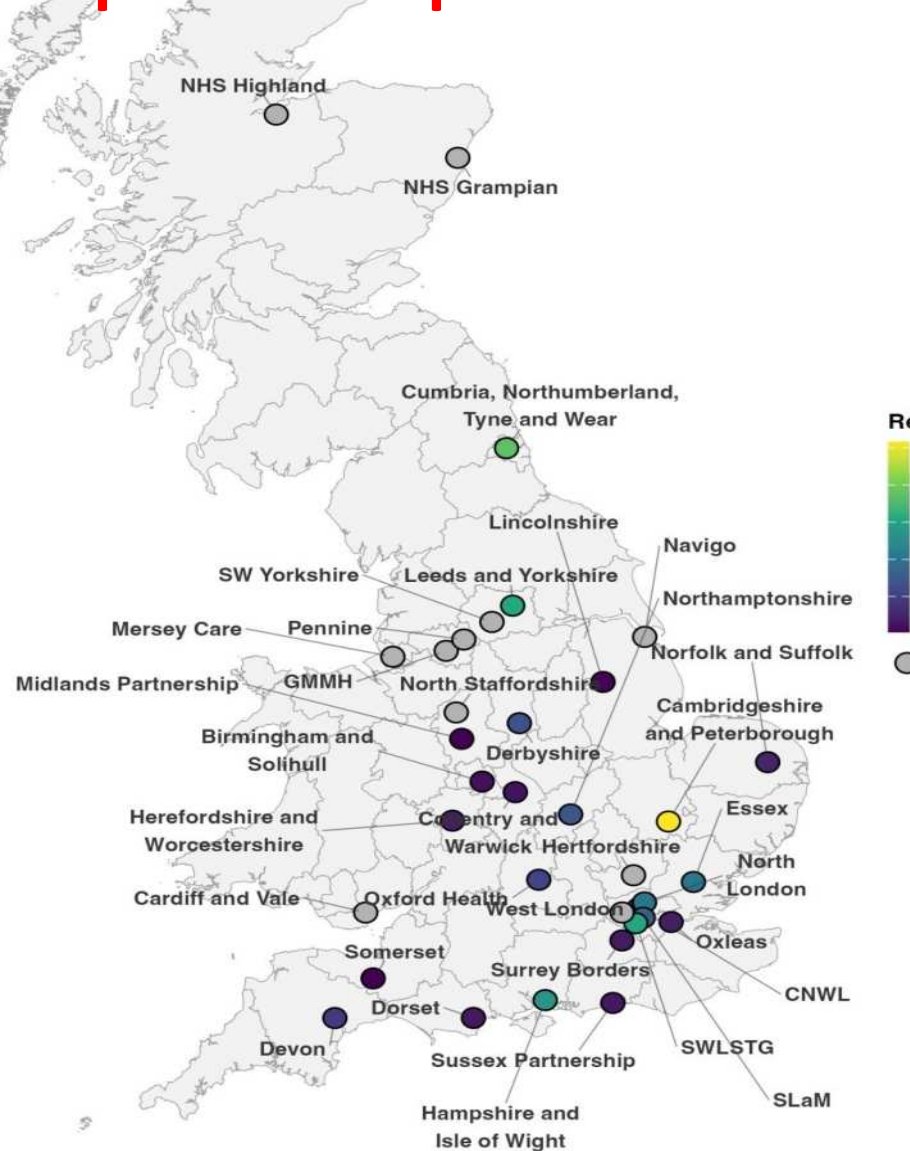
A single cohort study underpins the network, with consent to re-contact built in

Deep phenotyping leadership

Co-led from computational psychiatry at Oxford and affective disorders at Newcastle — the endpoint expertise sits inside the network.

Early Psychosis Network

First-episode, prodromal & complex schizophrenia



500+ participants in the Early Intervention Mission cohort

7 cities, NHS-embedded

Birmingham · Bristol · Cambridge · Cardiff · Liverpool · London · Manchester

EPICare, live in service

Research database inside routine NHS care

Trial platforms ready

PUMA platform trial + Complex Schizophrenia Clinic

What the networks de-risk

01 Feasibility first

Size your cohort on real criteria — before sites open

02 Precise enrichment

Subtypes, resistance & staging verified in the record

03 Lower placebo response

Trial-naïve regions, not “professional” participants

04 Endpoints in-house

Biomarker, imaging & digital phenotyping in recruiting clinics

All checkable before commitment.

The hard parts are already built

The infrastructure for mental health trials is in place

122 days

Avg. trial set-up (down from 169)

2m+

Consented in Our Future Health

20,000

Genomic samples (MHG / GLAD)

Regulatory

Extensive interactions with MHRA, NICE (seconded staff)

Not a capability gap Mental Health Goals Programme represents a major route in.

What industry has been asking for

Five major deliverables



Robust data & digital

One secure national data platform



Omics & phenotyping

20,000 genomic samples



Lived experience, built in

Patient-industry partnership



Regulatory alignment

MHRA, NHS & HTA from the start



Facilitated Entry

Single entry to UK expertise & trials

**UK well poised for
precision psychiatry
leadership**

- **Mental Illnesses are one of the most pressing health, economic and social justice issues of our time**
- Rx Dev has been slow, partly owing to reliance on traditional sx-based diagnostic frameworks which “lump” patients together.
- **After a long hiatus, we are turning the corner with a number of novel , improved mechanisms for specific px populations**
- Biomarker efforts will utilize patient-specific biological measures of brain function to ultimately facilitate targeted Rx dev.
- **We owe this to patients and families and take it on as a shared societal responsibility; UK leadership is apparent**

