A component of cannabis could hold promise as a new class of treatment for schizophrenia, according to King’s College London research showing significant positive effects on symptoms and illness severity.

The main active compounds found in cannabis are delta-9-tetrahydrocannabinol (THC) and cannabidiol (CBD), and while THC is thought to be responsible for some harmful effects, recent evidence suggests that CBD may protect against negative outcomes such as memory impairment and paranoia.

Although small case studies have pointed to the potential use of CBD in schizophrenia, this new research - published today in the American Journal of Psychiatry - is the first and largest study to compare CBD with a placebo.

Antipsychotic drugs have been the first line of treatment for schizophrenia over the last 60 years and although they are effective for many, treatment response is still poor in up to a third of patients. In addition, their beneficial effects are mainly on “positive” symptoms such as hallucinations and delusions, rather than on negative symptoms including poor motivation and reduced speech/activity.

One explanation is that negative symptoms may not be driven by elevated levels of dopamine in the brain, which is the key mechanism that antipsychotics seek to address. Therefore, researchers are urgently looking for treatments that work differently to antipsychotics.

In the King’s College London study, funded by GW Research, 88 schizophrenia patients received either CBD (one gram per day in liquid form) or placebo for six weeks, alongside their existing antipsychotic medication. Before and after treatment, researchers assessed the severity of schizophrenia symptoms, level of functioning, and a psychiatrist’s overall clinical impression.

Patients treated with CBD had lower levels of positive psychotic symptoms compared to those who received a placebo. The CBD group were also more likely to have been rated as “improved” and not severely unwell by a treating clinician.
There were also small statistical trends for improvements in cognitive performance and in the overall level of functioning, raising the possibility that CBD may have beneficial effects in this area too.

Professor Philip McGuire, lead author, said: “In patients who do not respond to antipsychotic drugs, we could assume their dopamine function is normal. If true, we need a drug that works differently and does not try to block dopamine receptors.”

Although it is still unclear how exactly CBD works, these early results are promising. Not only were these outcomes found in patients already receiving antipsychotics, showing that improvement in symptoms was over and above the effects of existing medication, the improvement was also reported by treating psychiatrists, highlighting that these outcomes were clinically meaningful.

“CBD also showed no side effects, which is especially significant given that antipsychotic medication can be associated with adverse effects in some patients”, Professor McGuire added: “We now need to carry out larger studies looking at the effects of CBD during different stages of schizophrenia, as well as exploring it’s potential application in other disorders such as epilepsy and attention-deficit hyperactivity disorder (ADHD).”

Research updates:

**Pioneering study helps people with schizophrenia control brain activity**

For the first time, new research shows people with schizophrenia can train themselves to control brain regions linked to verbal hallucinations, using an MRI scanner and a computerised rocket game. The pilot study by researchers at King’s College London’s Institute for Psychiatry, Psychology, & Neuroscience (IoPPN) and the University of Roehampton suggests the pioneering technique might help patients who don’t respond to medication learn to control their symptoms.

The study involved 12 patients who experienced verbal hallucinations on a daily basis. The hallucinated voices of 70% of people with schizophrenia hear cause a high level of distress and disruption to daily life, and medication is ineffective for around 30% of patients who experience these verbal hallucinations. There is a clear need for alternative treatments. Brain imaging experts Dr Natasza Orlov and Professor Paul Allen targeted a region of the brain which is sensitive to speech and human voices, and is hyperactive in people with schizophrenia and verbal hallucinations.

The researchers designed a “neurofeedback” technique, where patients in an MRI scanner could monitor their own neural activity in the speech sensitive region of the brain. Neural activity was represented by a computerised space rocket, and patients were instructed to land the rocket by bringing it down to earth. No explicit instructions were given to patients about how to move the rocket, instead patients were asked to develop and apply their own mental strategies to move it. This is the first time neuro-feedback techniques have been investigated for schizophrenia and verbal hallucinations.

After four visits to the MRI scanner, patients were able to induce neural activity in the speech sensitive region of the brain and were able to control their brain activity without the visual feedback from the space rocket. After training, patients had learned lasting strategies which they could apply during their daily lives.

Natasza said: “Although the study sample size is small and we lacked a control group, these results are promising. We are now planning to conduct a randomised controlled study to test this technique in a larger sample.”

Professor Shergill said: “Unfortunately, we don’t have effective treatments for all of the people with schizophrenia who hear voices and it’s great that this innovative research offers a novel approach to help patients with continued symptoms. While this is preliminary data, it’s particularly promising that patients were able to control their brain activity even without the MRI scanning - suggesting that this may be a strategy that people, who have followed the MRI neuro-feedback training protocol, can benefit from at home.”

**Early life risk factors and adult mental illness**

Research led by Dr Chiara Nosarti, showed that adults who were born prematurely (<32 weeks of gestation) have higher rates of psychiatric symptoms compared to adults born full term. This study assessed the type and severity of mental health symptoms experienced by adults who were born prematurely using the Comprehensive Assessment of At-Risk Mental States.

The participants born prematurely showed difficulties in concentrating, poor social functioning, delusions and racing thoughts. The findings in this study support the notion of a direct association between birth factors such as young gestational age and the risk of developing a psychiatric disorder later in life.

Dr Nosarti says: “A significant proportion of adults who were born prematurely, who may not have mental illnesses severe enough to warrant a diagnosis, continue to have higher than normal levels of mental health symptoms. The discovery of a potential mechanism linking early life risk factors to adult mental illness could lead to more targeted and effective treatments of psychiatric problems in people who experienced complications at birth.” New research funded by Action Medical Research is now looking at brain changes in childhood that could increase premature children’s risk of developing anxiety disorder. The study is also exploring whether specific features in brain scans collected around the time of birth could help to identify those children at greatest risk of mental health problems.

**Complications at birth associated with lasting chemical changes in the brain**

Research is shedding new light on potential mechanisms that increase psychiatric risk in people born prematurely, showing that in adult life those who also suffered small brain injuries around the time of birth have lower levels of dopamine in the brain.

This chemical change has been linked to lack of motivation and enjoyment in normal life, and changes to attention and concentration, which could all be early signs of more serious mental health issues such as depression. The researchers used a combination of positron emission tomography (PET) scans and magnetic resonance imaging (MRI) scans of the brain with a range of psychological tests in order to identify the precise changes to chemistry and structure of the brain following early brain damage.

They compared adults who were born very preterm who sustained early brain damage, to adults who were born very preterm who did not sustain brain damage and controls born at term. The study found that dopamine is affected in people who had early brain injury, but not in the way a lot of people would have thought - dopamine levels were actually lower in these individuals. The biological link between birth complications and greater risk of mental health issues is unclear, but one theory is that the stress of a complicated birth could lead to increased levels of dopamine, which is also increased in people with schizophrenia. Researchers believe these findings could help develop approaches to prevent the development of problems in people who were born early.

**Premature birth linked to older “brain age” in adult life**

New research suggests that babies born very prematurely show accelerated brain development in adult life, as their brains look “older” compared to people who were not born prematurely. The researchers analysed data from 328 MRI scans of very preterm people and 1442 MRI scans of controls.

The prematurity group had smaller volumes of several regions, especially those involved in memory and in processing emotions.

The study also revealed that some brain changes in areas responsible for complex reasoning are resilient to the effects of prematurity, possibly indicating the presence of compensatory mechanisms. As grey matter volume changes over the life span, it can be used as a marker of “brain age”. The researchers found that in the premature group there was a discrepancy between participants’ chronological age and “brain age” estimated from their MRI scan, suggesting that very preterm adults’ brains looked “older” than what would have been predicted by their age.

Dr Nosarti says: “It remains to be investigated whether these brain differences have real-life implications. If so, our results could inform the development of cognitive and behavioural interventions aimed at boosting brain resilience”.

**Illustration by Ali Gregory, Mount Sinai Health system.**
People who live in cities are at higher risk of a range of mental health issues. Yet it would be reductive to equate urban living with higher risk for mental illness, as cities can also have beneficial effects on mental health through increased opportunities for employment, socialization with like-minded people and access to specialised care. At present, we know little about the mechanisms through which urban living can negatively and positively affect mental health.

To investigate this issue, we developed Urban Mind – a smartphone app to examine how the built and social environments affect mental wellbeing in real time. The app uses a technique called “ecological momentary assessment” which involves sending participants notifications at random times and inviting them to answer a short series of questions about their current environment and mental state. In the pilot phase of the project, the app was used to monitor 108 individuals who completed 2013 assessments over a one-week period.

Our results indicate that brief exposures to specific natural features – such as trees, the sky and birdsong – have time-lasting beneficial effects on mental wellbeing. A single exposure to trees, for example, can lead to an improvement in mental wellbeing that is still evident seven hours later. An intriguing aspect of our findings is that these beneficial effects were stronger in people with higher trait impulsivity – a psychological measure of one’s tendency to behave with little forethought and a predictor of future risk of developing mental health issues. From a mental health perspective, these findings could inform the development of low-cost, scalable interventions aimed at supporting better mental health in urban populations. For example, prescribing regular access to green spaces could be a simple but effective way of helping city-dwellers at risk of mental health issues, maintain high levels of mental wellbeing and reduce future risk. From the perspective of urban planning and design, the results provide a much-needed evidence base that could inform future investments and policies. There is urgent need for such evidence since, at the present time, decisions on urban planning and design aimed at improving mental wellbeing tend to be based on “conventional wisdom” due to the lack of robust scientific data.

Having completed the pilot phase, we are now about to launch a large-scale investigation using an updated version of the Urban Mind app. This will be trial in the general population as well as clinical samples – which will collect both active and passive digital “markers” which could be used to predict clinical outcomes. We are inviting everyone to download the app and take part in this project. We hope the data will inform the development of novel clinical interventions and the planning and design of healthier cities.

Dr Andrea Mechelli
Reader in Early Intervention & Deputy Head of Department

Radical new approach to schizophrenia treatment begins trial

Professor Oliver Howes’s team is one of several worldwide to have uncovered evidence that abnormalities in immune activity in the brain may lie at the heart of the illness – for some patients, at least. During the next two years, 30 patients will receive monthly infusions of an antibody drug currently used to treat multiple sclerosis (MS), which the team hopes will target the root causes of schizophrenia in a far more fundamental way than current therapies. The trial involves treating patients with a monoclonal antibody drug, called Natalizumab, that is already licensed for MS. The drug works by targeting microglia and restricting their movement around the brain, which scientists hope could prevent the over-pruning of vital connections.

The first patient, a 33-year old man who developed schizophrenia after moving to London from Cambridge, was treated at King’s College Hospital last November, marking the start of one of the most ambitious trials to date on the biology of the illness and how to treat it. He received his first dose of treatment. He currently has monthly antipsychotic injections and his condition is now stable. He feels “on the way” to being himself again and is looking to (slowly) start working again. “It’s quite hard,” he said.

“In the past, we’ve always thought of the mind and the body being separate, but it’s just not like that,” said Howes. “The mind and body interact constantly and the immune system is no different. The most extensive pruning seems to occur in the frontal cortex, which may explain why patients often hear voices. The frontal cortex indirectly controls the brain’s levels of dopamine – a surge in this is thought to explain the delusions and paranoia experienced by those with schizophrenia.”

Belinda Lennox, senior clinical lecturer in psychiatry at the University of Oxford, said: “There’s a lot of emerging evidence that the immune system is going wrong [in schizophrenia],” she said. “If reducing inflammation acts to improve psychosis in this study it will open a new range of treatment possibilities, which is very exciting for the field, and desperately needed.”

Professor Oliver Howes
Professor of Molecular Psychiatry

MSc Mental Health Studies Prizes

Top students were awarded prizes by Dr Jenny Krasvati (Programme Leader) on the 24th January at the Education Hub.

Lydia Cartwright was the joint winner of the Nick Bouras Prize 2018 - Lydia completed a MSc Mental Health Studies at the IoP/PPN last year and she is currently supporting people living with brain injuries. “I also work as an ABA support therapist at the workshops and applied for Clinical Psychology training starting in September 2018.”

Abigail Affrey winner of the Jim Watson prize 2018, also completed the MSc last year and is now training to be a Clinical Psychologist at the Salomon’s Centre in Kent. “The course was great preparation for Clinical Psychology applications and training. Thank you so much to all the staff and students who made studying at King’s so rewarding.”
Dr Conrad Iyegbe
Postdoctoral Researcher

WP Grants Scheme – “Worldwide Partnership Fund”

The WP Grant Scheme provides seed funding to widening participation initiatives using the expertise of King’s staff. Bids are invited for £2,000 - £10,000 to run projects targeting widening participation learners, supporting access, transition or student success.

In collaboration with Student Advice Service, King’s Family Association, which I first founded here at the IoPPP, were awarded £5,000 to support student families at King’s. We proposed to use the money to execute a research project which would investigate how many of our students have additional family responsibilities and what sort of support they require. At present, we have no way of knowing how many of our students fall into this category.

Students with additional family responsibilities are more likely to drop out before completing their course and also report a poorer university experience, often being excluded from student events due to their responsibilities. To help with this social exclusion, we also proposed organising regular events for students and their families to connect in a relaxed way.

We are providing monthly family friendly activities (at the moment it’s yoga) as well as parties at Christmas and in the Summer.

Organising this society has been quite a challenge for me, juggling a PhD, two-part time jobs and a family has certainly honed my organisational skills. At the end of last year, I stepped down from my role. I was delighted however to have been nominated for a Student and Education Directorate Award. This was for my work in forming the Family Association and successfully receiving funding to support students.

I hope that the Family Association will continue to support student families and help to make King’s a family friendly space and accessible for all.

Elizabeth Appiah-Kusi
PhD Student

Diversity & Inclusion

The DfI SAT meets every 6 weeks to implement, promote and monitor objectives and strategies designed to improve the working environment for all staff and students.

Salary Negotiation

To equip staff with knowledge and skills based on salary negotiation techniques, the Pay, Promotion & Recruitment working group is developing an online Negotiation Toolkit to launch in January. This is one of a number of measures being introduced to try to address the gender pay gap within the institution.

Parenting rooms available at all campuses

The parenting room at the Franklin-Wilkins Building is now open. This means we have a parenting room at each campus; all are open to staff, students and visitors. Details available at https://www.kcl.ac.uk/for-staff-and-students/family-room.

Extension of academic life support for post-docs

At the end of their fixed-term contracts, post-docs who do not plan to move to another academic institution may be offered an honorary contract with King’s. The benefit of this is that it secures post-docs long term access to important research and educational partnerships.

Dr Conrad Iyegbe
Postdoctoral Researcher

#ChoosePsychiatry event at the Royal College of Psychiatrists

The Royal College of Psychiatrists is running a “ChoosePsychiatry campaign aimed at getting the brightest and best medical students to pick this specialty.”

The President, Wendy Burn, and Dean, Kate Lovett, are leading this across the UK running events at medical schools and “PsychSocs”. On February 7th, they held their largest such event, for 400 medical students at Bart’s Hospital London.

Dr Derek Tracy, visiting Senior Lecturer from the department, and Consultant Psychiatrist and Clinical Director at Orleans NHS Foundation Trust, gave a talk on the “evolution of consciousness”.

The event concluded with a talk by Stephen Fry, the President of MIND, who spoke of his own battles with mental illness, how psychiatrists had enormously helped his life, and why the best junior doctors should choose this specialty.

#ChoosePsychiatry event at the Royal College of Psychiatrists

The theme of the event was “Current Developments in the Genetics of Psychosis – Where do we go from here?” It attracted over 200 attendees each day. Winning this award has been very enabling for the development of the pilot study, which starts later this year. It also places me in a stronger position to compete for research council money to fund a much larger initiative, covering a much larger region. The motivating goal of this initiative is to secure global equity in the development and the application of precision medicine tools for psychiatry. More details about the Worldwide Partnership Development Fund can be found at https://www.kcl.ac.uk/about/International/International-Funding-Opportunities/PartnershipDevelopmentFund.

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Dr Conrad Iyegbe
Postdoctoral Researcher
Oliver Howes “Researcher of the Year 2017” Royal College of Psychiatrists

Oliver Howes, Professor of Molecular Psychiatry at the Institute of Psychiatry, Psychology & Neuroscience, and the London Institute of Medical Sciences, Imperial College London, was named R N Jaicoo Memorial Academic Researcher of the Year at the Royal College of Psychiatrists Awards.

Professor Oliver Howes is a Consultant Psychiatrist at the South London and Maudsley NHS Foundation Trust, where, amongst other things, he runs a service for people with refractory psychosis. He received the award from Professor Anne Lingford-Hughes, chair of the academic faculty at the Royal College of Psychiatrists.

Oliver said, “It’s a great honour to be recognised by the Royal College of Psychiatrists in this way. My research usually involves lots of people so this award is also testament to the many fantastic students and colleagues at King’s and the Maudsley who have helped with my studies. I am very grateful to them and the people who nominated me for their inspiration and support over the years. Most importantly, I’d like to thank the patients who motivate and take part in our studies.”

The review panel said, “Professor Oliver Howes has an outstanding track-record of research and scholarship. Through using positron emission tomography and magnetic resonance imaging, his work has significantly contributed to our understanding of dopaminergic and glutamatergic function in psychotic disorders.”

Oliver is a committed clinician and has developed guidelines to improve clinical management. He also mentors a number of trainees in developing their careers.

MRC UKRI HDR Fellowship

Rashmi has been awarded a prestigious 3-year Health Data Research (HDR) UK Fellowship funded by the Medical Research Council. HDR UK (https://hdruk.ac.uk/) is a new initiative to develop cross-disciplinary healthcare research programmes using cutting edge data science in research centres throughout the UK.

Rashmi is a Clinical Lecturer in Psychiatry who has undertaken research using the Clinical Record Interactive Search tool (CRIS) to investigate clinical outcomes in psychotic disorders. He has developed natural language processing tools to extract clinical data from free text electronic health records (EHR) in the SLaM Biomedical Research Centre (BRC) Case Register. During his fellowship, he plans to link EHR data with passive smartphone activity data to predict clinical outcomes in first episode psychosis.

Broadening horizons: 2017 Medical Education Conference

The Medical Education Faculty Conference “GKT, King’s & Beyond: Broadening our Horizons”, is an annual event that brings together clinical, academic and professional services colleagues who contribute to teaching and delivery of the medicine programme and recent graduates.

Professor Nicola Philips, Vice-President and Vice Principal (Education) gave the keynote speech followed by an awards ceremony to recognise contributions to teaching excellence. Congratulations to Professor Paola Dazzan who received the “GKT Recognition for Outstanding Contribution to Student Experience”.

Research Grants & Publications

Research Grants

  - Funder: Action Medical Research: £174,035.00
  - Funder: MRC - Medical Research Council: £78,460.00
  - Funder: MRC - Medical Research Council: £326,858.00
  - The effect of cannabis on brain function in cannabis users: without psychosis – addition of an important control arm to the EIGP study. Bhattacharyya, S., Sami, M.
  - Funder: The Dowager Countess Eleanor Peel Trust: £14,914.00
  - From brain to cell and back again: determining the molecular mechanisms of psychosis and developing a cellular platform for novel drug discovery. Srivastava, D., Howes, O., Vernon, A.
  - Funder: MRC - Medical Research Council: £50,000.00
  - A pilot study to link cortical interneuron dysfunction and striatal hyperdopaminergia in mice. Marin, O., Rico, B., Howes, O.
  - Funder: MRC - Medical Research Council: £50,000.00
  - International Research Programme on Psychosis in Diverse Settings (INTREPID II). Morgan, C., Murray, R.
  - Funder: MRC - Medical Research Council: £1,993,070.00
  - Understanding the biological mechanisms associated with anxiety in very preterm children. Nosarti, C., Counsell, S., Happe, F.
  - Funder: Action Medical Research: £185,999.00

Publications


