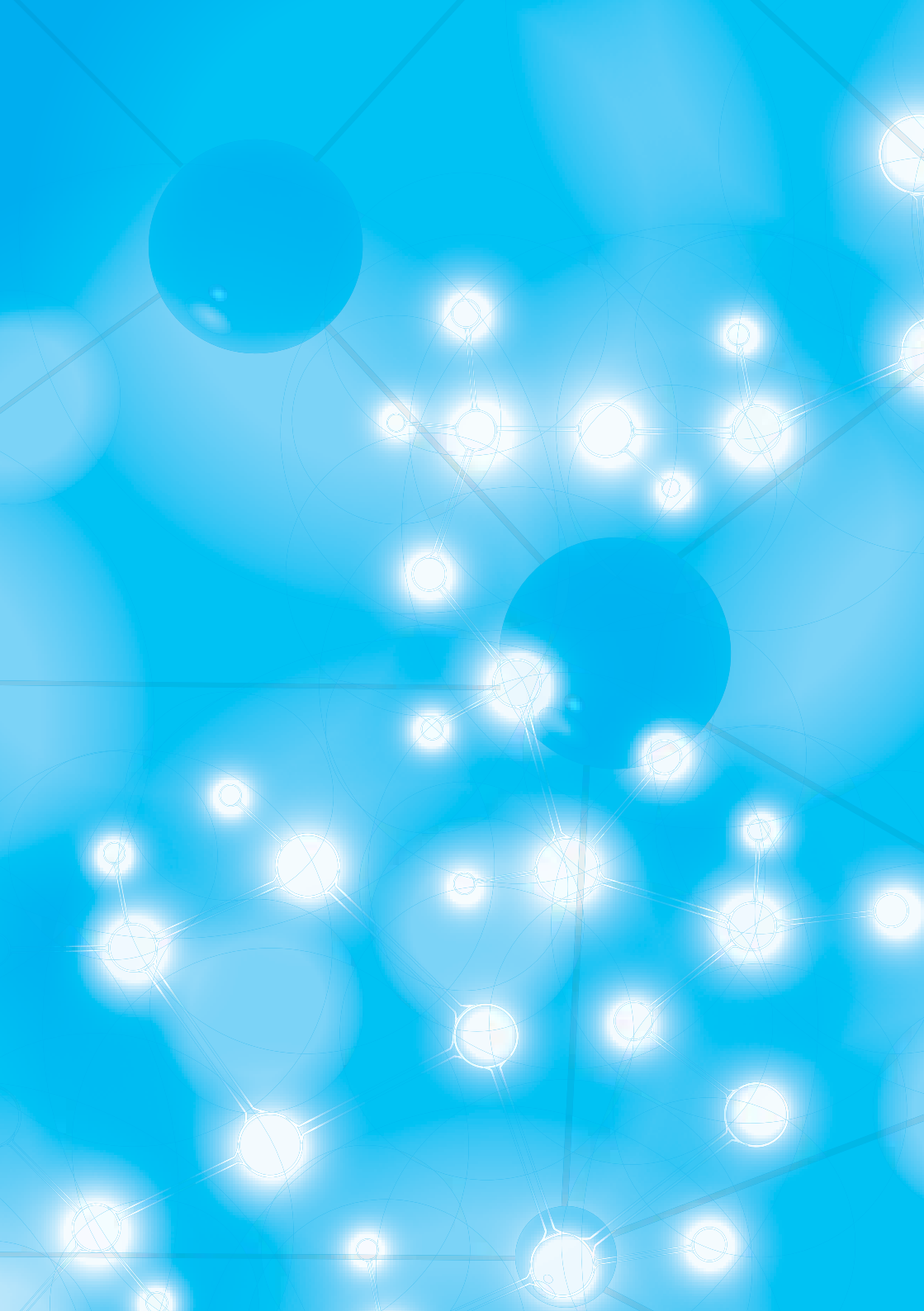


Antibody Mediated Psychosis

An Introduction to the Causes and Treatment

**Study of ImmuNotherapy in
Autoantibody Positive Psychosis**





Booklet Guide

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What is antibody mediated psychosis?

Introduction

Have you or someone close to you been diagnosed with antibody mediated psychosis? Perhaps you are just curious about the causes and treatment of the disease? As a sufferer myself and desperate for more research and resources on the subject, I have compiled this booklet.

Antibody mediated psychosis includes both anti-NMDAR and voltage gated potassium channel (VGKC) encephalitis, although many other related diseases are being identified.

I attempt to give a detailed but easy to understand guide of the disorder, what it is, what happens in the body and what we can do about it.

You can read more about me on page 18.

I hope that you find it helpful.

Sarah

July 2016



Causes of psychosis

Our perception and reaction to the world around depend upon what is happening in our brains.

Psychosis is a mental health problem signified by 'hallucinations' and 'delusions'. Hallucinations occur when we experience things that aren't really there – whether through sound, taste or sight. Delusions have more to do with how we think – we can become suspicious, irrational and have racing thoughts. Changes in mood and personality, odd or violent behaviour can also be part of a psychotic episode.



The causes of psychosis are varied. Drug and alcohol abuse can effect the brain and lead to psychotic behaviour. People with psychosis may also have diagnoses of schizophrenia or bipolar disorder. Occasionally the cause is our own body attacking the brain. Special Y shaped molecules called antibodies that normally protect us can become confused and attack healthy parts of the body. Therefore it is called 'antibody mediated psychosis'. This is an 'autoimmune' disease as the body's own immune system turns on itself.

For more information on psychosis see:
www.nhs.uk/conditions/psychosis.

The after-effects of psychosis?

Experiencing a psychotic episode, whether your own or someone else's can be incredibly devastating. Even if the episode itself is short-lived, there can still be a long road to recovery and acceptance.

Treatment depends on the progress of the psychosis and how ready you are to deal with it. I have experienced being sectioned on an acute psychiatric ward, had massive support from the Early Intervention Team including cognitive behavioural therapy and family therapy at my own home and also spent some time on a ward designed for people with mood disorders. The care is incredibly people-centred and designed around your own needs and situation.

Even with a neurological diagnosis such as antibody mediated psychosis, some mental health therapies and treatments may also be introduced to help manage symptoms and repair the emotional damage psychosis can cause.

For information on other people's experiences, please see www.healthtalk.org.

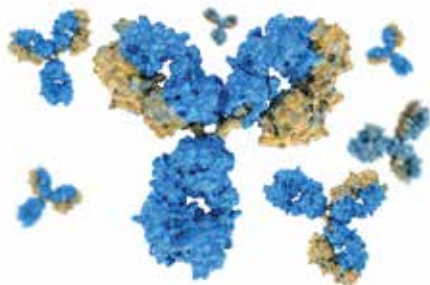
For more information on Early Intervention Services, please see www.mentalhealthcare.org.uk/early_intervention_services or www.nhs.uk.

Symptoms of antibody mediated psychosis

The type of antibody mediated psychosis depends on the type of antibody causing the disease. Each type has its own unique set of symptoms, but most follow a similar pattern. Quite often we experience flu-like symptoms first. Headaches, tiredness, fever etc. This could be several weeks before the mental health symptoms begin to surface, such as psychosis. At this stage, psychiatrists become involved, and you may be kept on a ward or put on certain types of drugs, often antipsychotics.

As the disease progresses, more physical symptoms can follow. These include seizures or fits, abnormal movements (particularly twitches in the face), extreme tiredness or vacantness. The antibodies also attack parts of the brain linked to memory and reasoning skills. This can lead to long- and short-term memory problems, poor concentration, motivation and sequencing when trying to do daily tasks like shopping and washing.

In some people, the illness progresses to involve different parts of the brain – ‘encephalitis’ which can lead to an unresponsive coma-like state. At this stage, it becomes clear something very serious and not necessarily psychiatric is going on. The body may attack part of the brain that controls breathing, leading it to fail, so many patients end up in the intensive care unit (ICU) in hospital.



Diagnosis of antibody mediated psychosis

The order and intensity of the symptoms differ from disorder to disorder and patient to patient. Therefore, it can be difficult at first to diagnose what is going on. Some patients only display the psychiatric signs of psychosis with problems sleeping and with their memory. These patients are often misdiagnosed with schizophrenia, depression or bipolar disorder.

In some, but not all cases, a small tumour is the cause of the body's autoimmune response. This is usually what is known as a teratoma, a word for 'little monster', found in the reproductive organs. These usually non-cancerous tumours contain human tissue – hair, skin, sometimes eyes and teeth! – but also, more importantly, brain tissue. It is thought that the body tries to fight off this little monster but in the attempt confuses the body's own brain tissue with that of the teratoma.

When antibody mediated psychosis is suspected, diagnosis is fairly straightforward. A blood test to check for which antibodies are causing the disease is vital. A lumbar puncture (in which a tiny sample of fluid that surrounds the brain and spinal cord is collected and tested for antibodies), an EEG to look at the electrical signals in the brain and scans of the brain and body (CT and MRI) to check for tumours may also be required.



Blood tests...

Scans...



Results!

It is important to catch the disease in its early stages. This is why people who experience a psychotic episode for the first time should be tested for antibodies. This is really key work.

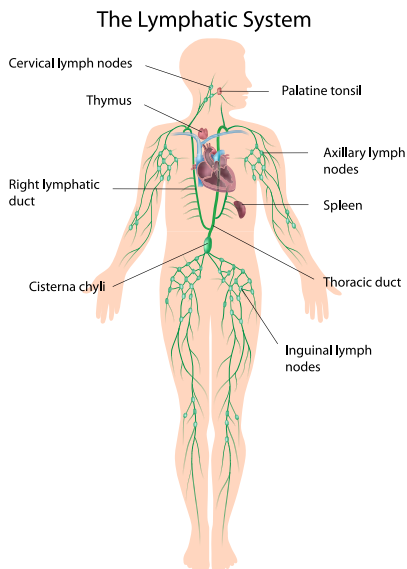
I was very fortunate to be tested by a research trial that happened to be going on where I lived. However, I was not officially diagnosed for a year after my initial psychotic episode.

What is happening in my body?

What is the immune system?

Inside our body are many groups of organs that work together to form systems. The heart, lungs and blood vessels make up the circulatory system. The mouth, throat, stomach and intestines make up part of the digestive system.

The immune system is the organs and structures that work to protect us against disease. Organs in the immune system include the tonsils, thymus, spleen, lymph nodes and bone marrow.



Cells in the immune system

Cells are the building blocks of our body. They contain all our DNA as an instruction sheet and work like factories – taking in raw materials, altering them and releasing them into the body.

When the body needs to defend itself against disease, the active cells in the immune system are formed from stem cells.

In addition to red blood cells that colour the blood, there are cells known as white blood cells are important in fighting disease. These travel through the blood and lymph system patrolling for infection or disease.

Many things can attack our bodies: parasites, viruses, bacteria and even seemingly harmless materials like pollen. So there are many types of white blood cells armed to fight different types of foreign material. Some directly engulf bacteria or the toxins they produce. Others produce molecules or chemicals to fight off infection.

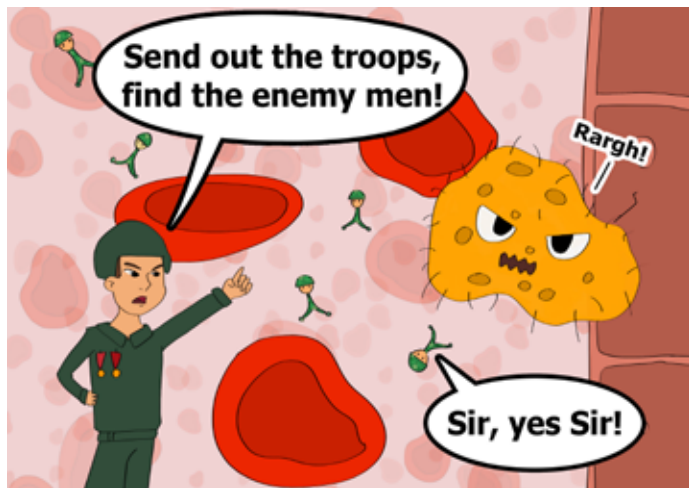
One type of white blood cell is a lymphocyte. There are two main subtypes of lymphocytes that are important in the immune system: B-cells and T-cells. T-cells come in two kinds. Killer T-cells destroy infections. Helper T-cells coordinate the attack on the infection.

It is the B-cells that produce and release antibodies. They can morph into two types of cell: memory cells and plasma cells. Memory cells recognise or 'remember' a certain kind of infection, which means our response to the same bad cells is much quicker the second time round.

It is the plasma cells that make antibodies and release them into the blood.

What is an antibody?

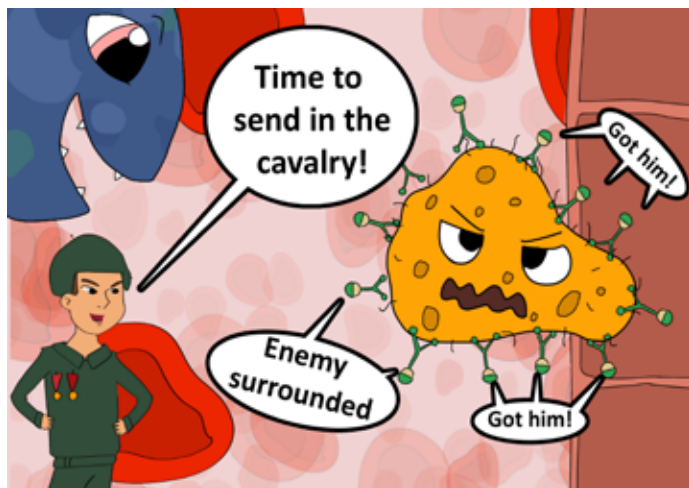
Antibodies are little Y-shaped molecules, or proteins, that patrol for bad cells through the blood. These antibodies work like the foot soldiers of our bodies' defences. They are on a seek and destroy mission.



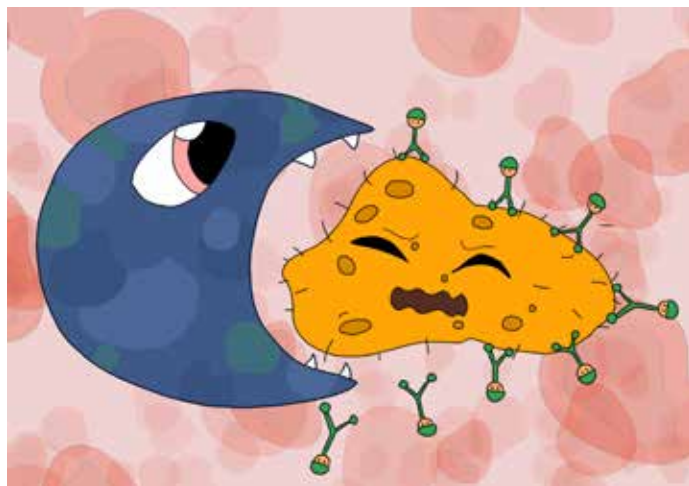
With special sticky 'feet', they recognise and attach themselves to bad cells like viruses or bacteria.



They have a special shaped 'hat' that attract larger bacteria eating cells.



These come and destroy the bad cells by swallowing them whole!



Different types of antibodies have different sticky feet to find and attach to different types of bad cells. Bad cells are clever and always changing shape, so the body needs to keep producing lots of different types of antibody soldiers to keep the body safe.

How do antibodies cause disease?

Antibodies are designed to fight disease. However, sometimes they become confused and attach to healthy tissue. The body responds by attacking itself at these sites, leading to inflammation and damage. This is what causes pain and swelling in the joints of those with rheumatoid arthritis.

In the case of antibody mediated psychosis, the brain becomes the target. Encephalitis literally means ‘brain swelling’.

The brain is the control centre of the body, maintaining physical, mental and emotional well-being. The brain and the body communicate through nerves – acting like wires in a circuit – sending electrical signals between the two.

Nerves within in the brain, are separated by gaps called ‘nerve junctions.’ These act like switches, either sending the signal on to the next nerve or stopping it.

Everything from the way we breath, the way we learn to how we feel and perceive reality is controlled by whether these signals are switched on or off correctly.

For a more in-depth look at nerves and nerve junctions, go to the 'Further information' section on page 20.

So how do the antibodies mess up the system? Basically it's to do with these nerve junctions or 'switches' in our bodies' circuits. Whether a switch is on or off in the brain is controlled by molecules called receptors.

Antibodies can attach to the switch and hold it open when it should be closed and vice versa changing the signal. They can also reduce the number of receptors controlling the switch.

This mixes up all the messages the brain is trying to send to the body, leading to swelling and an array of symptoms including psychotic behaviour.

Imagine a computer virus attacking the system that controls the traffic lights in a busy city. Think of all the accidents and confusion if when some lights were meant to be red, they turned green or if some traffic lights disappeared altogether! It would be totally disastrous.

This is what can happen when antibodies go wrong.

What can we do about it?

Treatment works by removing any tumours and the antibodies and temporarily reducing the body's ability to produce more. Normally, a combination of drugs (known as immunosuppressants) is prescribed alongside treatment in hospital such as IVIg or plasma exchange. Sometimes drugs called steroids are given to treat the inflammation of the brain.

Don't worry – these procedures sound a lot scarier than they actually are. They only require about a week in hospital and the drugs that you will be started on can normally be taken at home. So what is IVIg and what drugs can you expect to take?

What is plasma?

Blood is a mixture of plasma, red blood cells and other molecules. Plasma is a yellow-orange coloured liquid that carries these different cells and molecules in the blood through the blood vessels.

IVIg (Intravenous Immunoglobulins)

Intravenous is another way of saying directly into the veins. Immunoglobulins is another word for antibodies.

This treatment is like fighting fire with fire. It is the support, reduction or change of the immune system by introducing new antibodies into the blood.

The antibodies are collected from thousands of blood donors.

The procedure

Special antibodies are put into the blood through a drip. These antibodies can bind to B cells that produce our own antibodies and so control their release in the blood.

How this happens is not fully understood yet.

The antibodies are usually given through a vein in the arm through a cannula. Treatment takes a few hours and is repeated over three days.



Side effects and complications

The human antibodies can cause an allergic reaction in some people. The drip is run slowly to begin with and a nurse will monitor you carefully throughout.

The signs of a reaction are swelling of the face, breathlessness, headaches or a rash. Usually even if a reaction happens, it is only temporary and treatment can continue at a slow rate.

IVIg causes the blood to thicken. Therefore there is a high risk for those with a history of blood clots, stroke or heart disease.

This procedure has also rarely been associated with kidney problems and severe, persistent headaches.

Alongside IVIG, there is another procedure called plasma exchange (sometimes known as plasmapheresis or 'PLEX'). With PLEX, the plasma containing the harmful antibodies is exchanged for a plasma substitute. This is done using a special machine. The procedure takes around 2-3 hours. The procedure often has to be carried out a few times to be effective.

Don't panic!

Although these procedures sound quite scary, they are straightforward, safe and relatively painless. Many autoimmune disorders are treated this way.

IVIg is only a temporary fix. The effects can wear off after several months.

However, they are useful to confirm that it is the antibodies that are causing the problems and control the symptoms while we wait for the drugs to kick in!

A different, longer lasting treatment is then needed to stop the antibodies from coming back.

Monoclonal antibodies

Rituximab is a drug from a group of drugs known as monoclonal antibodies. It is also a chemotherapy agent used to treat skin cancer and lymphoma.

Like IVIG, rituximab is a concentration of antibodies, although

just a single type. These are collected from people and sometimes animals like mice, so there is a risk of a strong allergic reaction when getting this drug.

It is delivered straight into the veins, but takes a much longer time (around 6 hours). The drug has to be given slowly to reduce the likelihood of an allergic reaction.

There are usually three separate doses given. The first two are two weeks apart and then there is a booster dose six months later.

Rituximab works in the body by binding directly to B cells and killing them. It is therefore a very effective treatment although it can seriously weaken the immune system as a whole.

Side effects are nausea, vomiting, tiredness and increased risk of infection.

Rituximab is damaging to unborn babies, so it must not be taken during pregnancy.

For more information, please see
www.arthritisresearchuk.org/arthritis-information/drugs/rituximab.aspx.

That's it for now!

There is a lot of uncertainty about this disease, but great strides are being made in research all the time. Perhaps you could be part of the process of solving this puzzle!

I hope you found this booklet helpful! I know I said that's it but there is a further information page and a glossary to come! If you have any feedback or suggestions about what else should be included in this booklet, don't hesitate to get in touch!

I thought I could finish by giving you a quick summary of my experience, which you can read or skip altogether!

My story

In late 2013, I woke up on a consultation floor, the taste of an unknown drug in my mouth, with no hair, no memory of how I got there and no shoes. My mum was there. She looked both weary and wary in equal measure as if I might attack someone again. Or walk around naked. Or try to harm myself. Or hallucinate. Or a number of other disturbing things I'd done in the past ten days.

Somehow I had fallen from an active 22 year old, working as a carer and studying chemistry at Oxford, to a very strange place. But this was a fall I might never recover from. And what caused it? Well, in a way, it was me – my own body attacking my brain.

We had no idea what had caused the episode. Not knowing was just as bad as the actual experience. One day there was a knock on the door. I was asked if I wanted to take part in a research trial. They weren't looking to make any diagnosis, simply to compare their new test for these things called antibodies against the old one. It was a research trial that would literally save my life.

Even after a positive blood test result, it wasn't clear if I had NMDA encephalitis or not. I had a mass of investigations.

Nothing came back positive. Not even a second blood test. After months of waiting for answers there was only one – you don't have this, it's probably a combination of bipolar and migraines. I remember crying in the consultation room, not because bipolar is a bad diagnosis, but because of the sheer mental and physical exhaustion of being pulled from one answer to another and the uncertainty of it all.

Still to this day, even with a confirmed positive result, I am half suspicious of them taking it away from me. Thinking I'm a fraud or a phony. I know this is silly but there it is.

So what have I learned through receiving treatment? Patience springs to mind. This illness is a path less trodden at the moment but some research is making powerful steps to change this!

I'm still fighting this disease but know my story will end well. It's a hard road but at least I know which one I'm on!

Sarah, aged 25

Further information

How does the antibody cause disease?

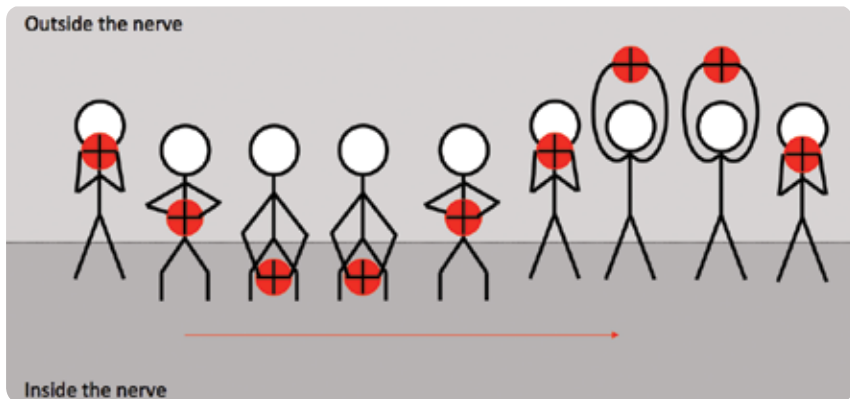
Antibodies usually fight infection and bad, foreign material in the body. However, sometimes they attach to normal tissue, leading to inflammation.

In antibody mediated psychosis, the antibodies attach to the nerves in the brain.

Nerves and ion gates

If the brain were a big computer controlling the body, then the nerves would be the wires conducting the signals.

Nerves are like very thin tubes. Changes in charge inside the nerve help send signals along in a wave. Special gates on the outside



of the nerve control how many charged particles called ions are allowed inside.

Imagine a Mexican wave of charge. The charge changes down the chain leading to a signal.

Nerves can sometimes become overexcited, which stops the signal. Imagine everyone in the stadium standing up at once – there wouldn't be any wave!

The signal can also be stopped when the gates are stuck shut. This is like everyone being stuck to their seat and unable to stand up to make the wave.

Nerve junction and receptors

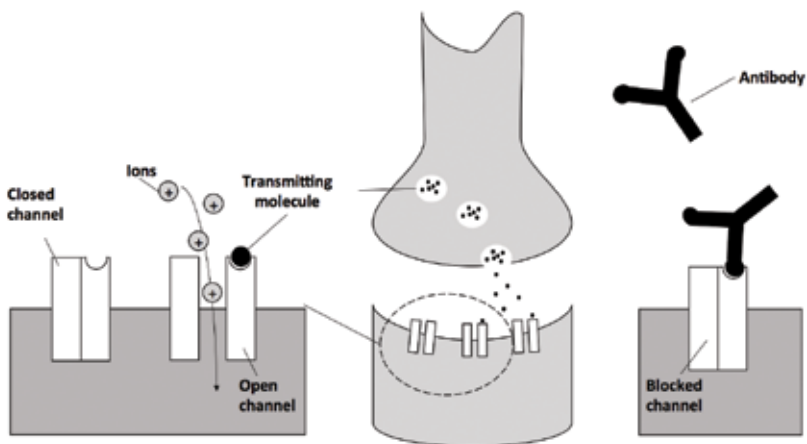
When two nerves meet, there's a little gap between them called a 'nerve junction'. This is like a little river between two areas of land.

To continue the signal, special molecules called 'neurotransmitters' cross the gap and activate the nerve on the other side.

There are special channels that the chemicals can fit into on the outside of the new nerve. It's like boats docking in harbours and unloading their cargo. These specially shaped 'harbours' are called receptors.

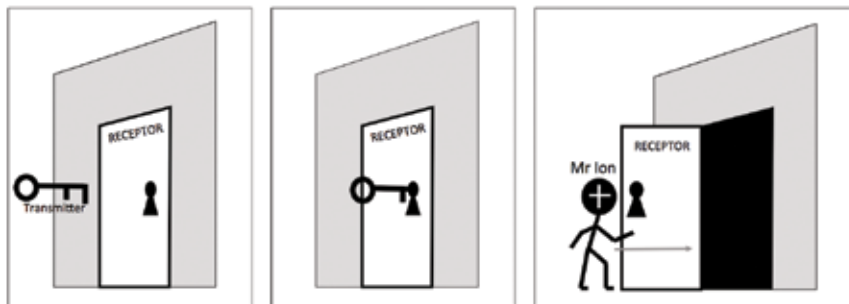
Receptors act like gates. When the boats are docked, the gate opens, so when the chemicals have successfully crossed the gap, they open up the new nerve to receive ions and start the Mexican wave all over again.

Certain antibodies can fill the harbour before the boat arrives without actually opening the gate. Therefore, antibodies 'block' or 'destroy' receptors and so stop signals from being passed on properly in the brain.



Imagine the receptors are like doors letting ions in and out. The chemical is like a key that exactly fits the keyhole in the receptor. They open the door and let ions in.

Antibodies work like a broken key in the lock, they have the right shape to fit but can't open the door. In fact they block it completely.



Useful resources

Resources about antibody mediated psychosis or encephalitis

The SINAPPS research group

www.sinapps.org.uk

The SINAPPS group is a collaborative research team that studies the role of antibodies in psychosis. The group will be carrying out a study testing IViG and Rituximab as a treatment for antibody mediated psychosis across England from 2017 onwards. This study is funded by the Medical Research Council (www.mrc.ac.uk). The study has received ethical approval from the South Central – Oxford C Research Ethics Committee (reference 16/SC/0584).

See www.sinapps.org.uk/studies for more details.

The Encephalitis Society

www.encephalitis.info

The Encephalitis Society produces many useful resources for service users. They also operate a helpline for people affected by encephalitis (01653 699 599).

The Anti NMDA Foundation

www.antinmdafoundation.org

The Foundation is a Canadian non-profit organisation.

The National Health Service (NHS)

Dial 999 in an emergency. Dial 111 if it's less urgent.

The NHS Choices website (www.nhs.uk) has a wealth of information about all areas of mental health. The website has a dedicated section on psychosis (www.nhs.uk/conditions/psychosis).

The website has a searchable database of NHS services throughout the country.

Charities

Mind (www.mind.org.uk) is one of the largest mental health charities in the country. There is a network of local Mind associations across the country. Mind operates a national information helpline called 'Mind Infoline'. Tel: 0300 123 3393.

Rethink Mental Illness (www.rethink.org) is a major mental health charity. Rethink Mental Illness runs many mental services and support groups. Rethink Mental Illness provides a helpline called the 'Rethink Advice and Information Service'. Tel: 0300 5000 927.

The Samaritans (www.samaritans.org) provide a non-judgemental free and confidential listening service. The service operates 24 hours a day all year round. Tel 116 113 or email jo@samaritans.org.

Videos

A video showing how antibodies defend the body from harmful intruders.

<https://www.youtube.com/watch?v=lrYIZJiuf18>

A video featuring Susannah Callaghan titled 'Autoimmune Encephalitis: Patient Perspective'.

<https://www.youtube.com/watch?v=82cvjItbCyY>

A Cambridge-based group called the Naked Scientists interviewed SINNAPS researcher Prof Belinda Lennox in 2013. The interview is titled 'Can antibodies cause schizophrenia?'

<https://www.thenakedscientists.com/HTML/interviews/interview/1000334/>

Glossary

Allergy/Allergic: To have a bad reaction when something is introduced. This can include a rash, difficulty breathing, a fever and trembling.

Anaesthetic: Used to numb pain or put you to sleep during a procedure. Local anaesthetic is where you stay awake. General anaesthetic is where you go to sleep.

Antibiotics: Medicine used to treat bacterial infections.

Antibodies: Y-shaped proteins in the body that help fight disease.

Autoimmune: A process during which the body's immune system attacks healthy tissue.

Bacteria: Small cells with no nucleus that can multiply and live in the body. Sometimes cause infection.

Bipolar Disorder: A mental health disorder that leads to dramatic highs (mania) and lows (depression).

Cannula: A way of getting drugs directly into the veins through a thin plastic tube and valve.

Centrifuge: A machine that is used to spin samples (for example, blood) in a circular motion around a fixed point.

Chemical: A pure form of one type of substance that has certain properties.

Chemotherapy: The treatment of disease using chemicals, particularly related to curing cancer.

Circulatory System: The organs in the body that distribute blood.

Clotting Factor: Also known as fibrinogen. A small protein that flows in the blood throughout the body.

CT (Computed Tomography) Scan: A way of imaging certain tissues using minimal radiation.

Depression: A mental health disorder sometimes caused by an imbalance of chemicals in the brain that produces symptoms such as low mood, fatigue and suicidal thoughts.

Dialysis: A procedure in which a patient's blood is filtered by a machine to remove bad things in the blood and relieve disease symptoms.

Digestive System: The organs that break down and process food and drink in the body.

Disease: A problem with a plant, animal or human that negatively affects their function or structure leading to a certain set of symptoms.

DNA: A particular chemical that controls the growth and development of most living organisms. DNA contains most of the genetic information within cells.

EEG (Electroencephalogram): A non-invasive procedure that measures brain waves using electrode pads attached to the head.

EIT (Early Intervention Team): A free service available for those suffering from psychosis for the first time.

Encephalitis: Literally means 'brain swelling'. Can have a number of causes including viral or bacterial infection or autoimmune disease.

Family Therapy: A talking treatment to include carers and relatives who have been affected as well as the patient.

ICU (Intensive Care Unit): One-on-one care provided for the very sick in hospital.

Immunoglobulin: A fancy word for an antibody.

Immunosuppressant: A chemical that reduces the effects of the immune system.

Infection: Sickness caused by an invading substance in the body.

Inflammation: Unnatural swelling or growth.

IV (Intravenous): 'Into the veins', how drugs are given directly into the circulatory system.

IVIg: See page 14.

Lumbar Puncture: A procedure in which a sample of the fluid around the brain and spinal chord is collected through a needle into your back. Local anaesthetic is used.

Lymphocyte: One type of white blood cells.

Memory Cell: A type of B-cell that keeps antibodies fighting an infection that has already occurred in the body.

Molecule: A group of elements connected in a chain by particular bonds.

Monoclonal The formation of a cell as a clone of a single parent cell as opposed to two or more.

MRI (Magnetic Resonance Imaging): A way to image the inside of your body.

Nausea: Feeling like you're going to be sick.

Nerve junction: Where separate nerves meet each other.

Nerves: Long, thin structures in the body that carry electrical signals around the body.

Neurology/Neurological: The study of nerves.

Oral: By mouth.

Osteoporosis: A disease in which the bones become less dense and more brittle. Tends to be noticed when a fracture occurs.

Parasite: A small living creature that lives off another living creature.

Peripheral: Way out of the centre of focus, like peripheral vision. Peripheral veins are found in the arms and legs.

Plasma: A yellow-orange liquid that forms roughly half the volume of blood.

Plasma Cell: The antibody factories of the body.

Plasma Exchange: A process whereby the plasma part of the blood is separated and removed to be replaced by donor plasma.

Protein: A structure made up of a chain of small units called amino acids that are bonded together to give a particular shape.

Psychiatry/Psychiatric: The study and treatment of mental illness and related emotional and behavioural issues.

Receptor: A structure in the body that detects and reacts to the presence of a specific molecule or chemical.

Rheumatoid Arthritis: An autoimmune disease of the joints.

Schizophrenia: A long-term mental health condition that affects people's understanding of themselves and reality.

Stem Cells: Cells that can change into any given cell of a particular organism.

Stroke: An attack caused by lack of oxygen in the brain that leads to quick cell death and disability.

Symptom: A physical, mental or emotional indicator of disease in the body.

Teratoma: Means 'little monster'. A benign (non-cancerous) tumour containing various human tissues.

Tremor: Uncontrollable shaking, usually in hands.

Ulcer: A fungal infection that commonly occurs in the mouth leading to small, painful blisters.

Virus: A small collection of DNA-like material in a protein coat that can infect and multiply in living cells.

Get in touch!

If you have any comments or suggestions, then please do get in touch.

Email: sinapps@psych.ox.ac.uk

Web: www.sinapps.org.uk and
www.antibodymediatedpsychosis.org

Twitter: @AMPsychosis

Funding

This booklet was produced using funds from research grants provided by the Stanley Foundation and the Medical Research Council.



The
Stanley
Foundation

MRC

Medical
Research
Council

Disclaimer

While we have taken every effort to ensure that the information in this booklet is correct at the time of writing, we cannot be held responsible for any errors that this booklet may contain.

A great deal about antibody mediated psychosis simply isn't known. It is very possible that since the publication of this booklet more will be known about antibody mediated psychosis and what the best treatments for it are. In other words, things may very well change.

We would always encourage you to seek professional medical advice if you have any questions rather than rely on the contents of this booklet.

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Version 1.0. Booklet produced September 2016.

Design: White Halo Design Ltd – www.whitehalo.co.uk

Illustrations on pages 10 and 11: Sarah Bates – www.sarahandtheStrange.com

About the McPin Foundation

The McPin Foundation is a mental health research charity. We champion experts by experience in research so that people's mental health is improved in communities everywhere.

- We deliver high quality user focused mental health research and evaluations.
- We support and help to shape the research of others, often advising on public and patient involvement (PPI) strategies.
- We work to ensure research achieves positive change.

The McPin Foundation is providing the service user and carer input into the SINAPPS study. To find out more about McPin, please visit www.mcpin.org, email: contact@mcpin.org.

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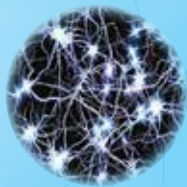
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**Study of ImmuNotherapy in
Autoantibody Positive Psychosis**

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