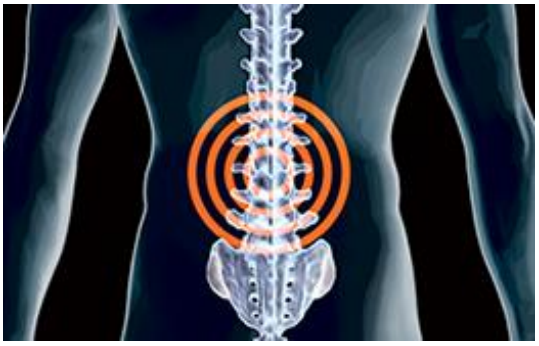
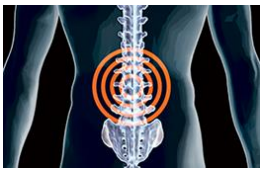
ABPP Study

A Study of Low Back Pain and Autoimmune Factors



Information Leaflet
2021

ABPP



A Study of Low Back Pain and Autoimmunity

We would like to invite you to take part in the Autoimmunity-Informed Phenotyping in Chronic Non-Specific Low Back Pain Sufferers (ABPP) study, set up by the Pain Research Institute in collaboration with the University of Liverpool, the Walton Centre and Aintree University Hospitals.

The study involves 100 participants who suffer Non-Specific Low Back Pain; low back pain that does not have an identifiable cause. The aim is to understand if this type of back pain shares similarities with other chronic pain conditions, and whether the immune system, the network of proteins that works to defend our bodies from infections and other injuries, plays a role. The study will also look into whether people with certain lifestyle and pain features are more likely to suffer from this type of low back pain. Participants will be asked to fill out a number of questionnaires looking at their pain symptoms, mental health and lifestyle, as well as undergo an examination and tests of sensation at the lower back and donate samples of blood for analysis of immune system markers. This is what we call 'phenotyping' – a process of identifying and assessing the measurable characteristics of individuals, and the hope is that we can use this to spot patterns in a back pain population. We hope the study's findings will provide a pathway towards better management and understanding of this painful condition.

Before you participate it is important you understand why the study is being conducted and what is involved. Please take some time to read through this information leaflet and discuss with others as you need.

If anything is not clear, or you would like more information, please call or email the study team through the contact details given at the end of this information leaflet. At your study date there will be a further opportunity to ask any questions you may have.

Thank you for taking the time to learn about the ABPP study.

Why is the study needed?

Non-Specific Low Back Pain (NsLBP) is back pain that does not have an identifiable cause, and will affect around 8 out of 10 people during their lifetime. For some this pain can be significant and long-term, affecting their quality of life, financial circumstances and social interactions. Despite the large number of NsLBP sufferers, we still do not yet fully understand the causes and risks associated with the development of this pain. Current treatment can be beneficial for some but many are left without appropriate symptom control.

Recent research from our group has identified the importance of immune factors in the chronic painful conditions of Complex Regional Pain Syndrome (CRPS – a pain condition that may develop after trauma in a limb) and Fibromyalgia (a widespread pain condition). These conditions are associated with severe pain on light touch/pressure and local skin signs such as increased sweating, or with widespread pain.

Some patients with severe NsLBP present with similar skin signs to CRPS, and NsLBP is a risk factor for the development of Fibromyalgia. We wish to find out whether a specific group of NsLBP sufferers may have similar signs and immune changes as those with CRPS and if sufferers can be identified early as being at particularly high risk for the development of Fibromyalgia. In addition, we wonder whether individuals who may suffer from immune-related pain share similar personal characteristics, such as pain scores or coping mechanisms. This study will provide blood samples for investigations into immune factors and cells, including their function and character related to pain, as well as analysis of DNA for genetic links.

We expect that this study will allow us, for the first time, to identify subgroups of NsLBP with similar immune abnormalities to CRPS or Fibromyalgia, opening new avenues for their future treatment.

What is involved if I take part in the study?

Taking part in the ABPP Study would involve:

- A video-link conversation to discuss involvement in the study. If a video link is not possible for you due to technical reasons, then this will be done face to face during the study visit and assessment
- Being asked to attend for a visit at the Clinical Sciences Centre, Aintree University Hospital, for a total duration between 2-3 hours
- Undergoing an examination of the lower back and limbs

- Testing the sensitivity of the skin at the lower back and arm – this will be performed using Quantitative Sensory Testing. More information on this process is provided below
- Assess the amount of sweating present at the lower back, using an iodine solution on the skin with starch powder applied over the top and analysis of the final colour change
- Completing a series of questionnaires around your mental health, social circumstances and pain symptoms
- Donate a blood sample with a volume up to a maximum of 12 tablespoons, or up to 180ml, which will be taken for storage and analysis into immune function and specific immune molecules related to pain
- The same blood sample will also be used for later DNA analysis aiming to identify genes related to pain conditions
- Agreeing to give the ABPP study team permission to access your medical and other health-related records and for anonymous storage and use of this information for other, ethically approved health-related purposes only
- Agreeing to have your questionnaire data and samples stored by the ABPP study team and used in the future, in an anonymous form by approved researchers both inside and outside of the study team, for a range of ethically approved studies
- Being invited back, if deemed appropriate by the study team, for a further optional 1-2 study days
- Being contacted one year following your involvement in the study for a telephone questionnaire follow-up

Quantitative Sensory Testing

In order to analyse the sensitivity of the skin at the lower back we will use a set of accepted and commonly used tests called Quantitative Sensory Testing, or QST for short. These are non-invasive, simple tests which look at how well the nerves that supply the skin are working. Nerves are like wires and sensory nerves pass information from the skin to your brain. In certain conditions, such as Complex Regional Pain Syndrome, damage to the nerves can result in changes to these information pathways. Understanding how easily you detect certain sensations and how intense these sensations are can help us gather important information about your low back pain.

There are four main types of sensation assessed during the test, and each one is performed a different way

- Temperature: a small device that produces temperature changes (hot/cold) is held against your skin. You will indicate when the sensations become hot or cold, and when they start to become more uncomfortable.
- Pressure: different weighted devices and/or material (such as cotton wool) will be held against your skin, and you will be asked to indicate

whether you can feel them or not. We will also use a blunt pressure gauge and you will indicate when the pressure starts to become uncomfortable.
- Pinprick: different weighted narrow-tipped devices will be held against your skin and you will be asked to identify whether they produce a sharp or blunt sensation
- Vibration: a device that produces vibrations will be held against your skin, and you will asked to indicate changes in the vibrations

We will also be testing the effect of uncomfortable sensations on each other, in this case cold water or ice applied to the skin, followed by a pressure sensation. We believe that in certain pain conditions, including low back pain, dysfunction in the body's ability to control these uncomfortable sensations may result in some of the symptoms you are experiencing.

The tests will take about an hour in total, with each test to be performed at the site of maximum pain in your lower back and at another site on your forearm. This site is the 'control site' and will be used to compare results to your site of pain. You will be lying down or sitting for the majority of the procedure and results will be entered into a computer which will produce graphs and tables for researcher analysis. These tests do not have any side effects and are not intended to cause significant pain or discomfort.

You mentioned additional tests or visits?

We believe that some participants may display certain signs during assessment that are similar as in the chronic pain condition CRPS – things like increased skin sensitivity to temperature or pressure. In 10 of these participants we will either carry out an additional test at the first visit or ask them to return soon after, during a time of maximal pain intensity. This additional test involves the painless formation of 3 small blisters on the skin of the back and forearm, using a suction cup device. This will take around 2-3 additional hours. The blisters formed are no more than 1cm in diameter. We will analyse the blister fluid for immune factors within the skin. Providing these additional samples, if you are asked, is entirely optional and will not affect your inclusion in the study. At this point we will also take another sample of blood, up to a maximum quantity of 12 tablespoons or 180ml, for storage and analysis.

We will also invite 30 different participants, selected from those who report a pattern of low back pain that occurs in 'flares' i.e. periods of acute worsening, for a repeat study visit at a time when they have a pain flare. This additional visit will involve taking another blood sample, up to a maximum of 12 tablespoons, and a further examination of the lower back.

Finally, 1 year after the first visit, we will telephone all participants and complete a remote questionnaire, in order to understand how their pain has progressed over the year. Based on previous evidence, we expect that 10-20 individuals of

the whole group will have developed certain widespread pains and we are interested in whether these pains may meet the criteria for Fibromyalgia. Participants invited for this final study visit (a maximum of 10-20) will donate another sample of blood, up to a maximum of 12 tablespoons, complete a questionnaire around Fibromyalgia diagnosis and be examined for Fibromyalgia features.

No participant will be asked to attend for every one of these visits mentioned. The maximum number of visits an individual will be asked to attend is two, while some will only attend for the initial study visit.

What will happen with my samples?

Blood and blister fluid samples will be securely handled. Each collection sample will be labelled using a unique study number with no identifiable information. They will then be transported by a member of the research team directly to the secure laboratories of the Pain Research Institute, where they will be analysed or frozen for storage and use in future research.

A small sample of blood will be stored for future DNA analyse by researchers at Cambridge University. This involves looking for specific genes that might increase your likelihood of suffering from painful conditions. This analysis will be completed at a later date.

Why have I been invited and am I eligible?

We are inviting sufferers of non-specific low back pain who attend back pain physiotherapy clinics at the Walton Health Centre and Aintree University Hospital. Or we may also have identified you through your inclusion in the Walton Clinic Pain Management Registry.

You <u>are eligible</u> to take part in this study if:

- You are 18 years or older
- You suffer from non-specific low back pain, without the presence of another condition to explain the pain such as musculoskeletal conditions, sciatica or cancer
- You suffer from chronic back pain, which is defined as pain on more than 4 days a week, for the past 12 weeks or more
- You experience weekly substantial pain that causes a significant disability
- Your pain may radiate down the buttocks or backs of legs but will not typically radiate below the knees
- If you experience pain in other parts of the body, your primary painful site is at the lower back

You <u>are not eligible</u> to take part in this study if:

- Pregnant or Breast-Feeding

- You have been informed by your doctor that you have an immune deficiency or are taking medications that may affect your immune system
- You have other substantial chronic pains that are worse than your lower back pain
- You cannot easily understand and communicate in English

What should I do if I want to take part?

If you would like to join the study, then all you need to do is contact the number or email the email-address listed at the end of this information leaflet. You will be able to ask any further questions you may have, and we will arrange a day and time that suits you, to either have the initial video-link meeting or to attend the study centre. Prior to any video-link meeting we will mail you a consent form which will be explained and completed on the day of the meeting should you agree to participate. This will then be returned via pre-paid mail to the study team.

Following completion of your consent to participate in the study, and prior to the first study visit, we will send the necessary questionnaires via email or mail. These may be completed prior to the visit, and you will bring them with you on the day.

If you do end up participating in the study, we will send a letter to your GP to inform them of your involvement.

Are there any benefits for me joining the study?

There are no immediate direct benefits should you choose to participate. However, we hope in the future that the information we discover can be used to improve the lives of everyone with non-specific low back pain.

We will provide a compensation of maximum £30 for travel and parking expenses per study visit.

Are there any risks for me joining the study?

You will be asked to donate a sample of blood during the study visit. Blood donation carries a minimal risk related to skin and muscle trauma. All steps will be taken to ensure your safety and the blood will be taken only by a registered healthcare practitioner. The formation of skin blisters is not a painful procedure, but there is a rare risk of infection, delayed healing of the blister sites which may very infrequently result in scarring and irritation at the site. If the extremely unlikely event that any concerning results are identified on your blood results we will contact your GP, with your consent, and they will arrange the necessary follow-up.

Some of the questions you will be asked to answer in the questionnaires may relate to sensitive topics and there is a possibility some individuals may experience distress as a result. If after completing the questionnaire pack you require support to discuss any sensitive topics you may call the Chief Investigator through his secretary for further advice on 0151 556 3391. Please note that although the Chief Investigator will aim to respond to you as soon as possible this is not an emergency service. If you require urgent support please visit A&E or ask your GP practise for an urgent appointment.

Participation in this study is subject to COVID-19 protocols. If you or any family members have symptoms or have tested positive we ask that you adhere to government self-isolation procedures. All effort has been made to reduce the risk for participants, with video linked contact whenever possible and personal protective equipment to be worn by research staff, but there is still a risk posed by attendance due to COVID-19.

How will we use information about you?

We will need to use information from you for this research project.

This information will include your:

- Initials
- NHS number
- Contact details

People will use this information to do the research or to check your records to make sure that the research is being done properly. People who do not need to know who you are will not be able to see your name or contact details. Your data will have a code number instead. We will keep all information about you safe and secure.

Once we have finished the study, we will keep some of the data so we can check the results. We will write our reports in a way that no-one can work out that you took part in the study.

Liverpool University is the sponsor for this United Kingdom based study and will act as the data controller. In the UK all research using patient data must follow UK laws and rules. These are the General Data Protection Regulation (GDPR) rules and the Data Protection Act. This study will adhere to these regulations. The Liverpool University will keep identifiable information about you for 10 years after the study has finished.

What are your choices about how your information is used?

You can stop being part of the study at any time, without giving a reason, but we will keep information about you that we already have. We need to manage your records in specific ways for the research to be reliable. This means that we won't be able to let you see or change the data we hold about you.

If you agree to take part in this study, you will have the option to take part in future research using your data saved from this study.

- All data gathered during the study visit, including physical examination findings and questionnaire responses, will be stored for a maximum of 10 years on a password protected hard drive, with your personal data only linked to your study number.
- Blood and blister fluid samples will be stored in the secure laboratories of the Pain Research Institute for a maximum of 10 years, and either used soon after your visit or frozen and stored, with only your study number as an identifier.

Where can you find out more about how your information is used?

You can find out more about how we use your information

- At www.hra.nhs.uk/information-about-patients/
- By asking one of the research team
- By ringing us on 0151-529—5835
- By contacting the Liverpool University Data Protection Officer, Mr. Daniel Howarth; via telephone during normal working hours on 0151-794-2148 or via email at Daniel.Howarth@liverpool.ac.uk

Can I withdraw from the study if I want to do so?

We encourage you to contact the study team if you have any concerns that you would like to discuss. However, it is completely up to you if you want take part in this study, and you are free to withdraw from the study at any point if you wish. You do not need to give a reason and there will be no change in your normal NHS back pain treatment.

You can withdraw by calling the study team, Monday-Friday or by emailing through the contact details given at the end of this document.

What if there is a problem?

If you have any concerns about any aspect of this study, please contact the study team who will do their best to answer any concerns (contact number given at the end of this document).

If you do not feel your concerns have been properly addressed following conversation with the study team, and you wish to complain formally, you can do this through the University Complaints Procedure. The contact number for Karen Wilding, the responsible officer at the University of Liverpool, is 0151 794 8373.

If you wish to raise a complaint on how we have handled your personal data, you can contact our Data Protection Officer who will investigate the matter. If you are not satisfied with our response or believe we are processing your personal data in a way that is not lawful you can complain to the Information Commissioner's Office (ICO).

Can I know the results obtained from my samples?

We do not currently have any plans to feedback results from you samples directly. This includes the DNA analysis that will be performed later. However, if we did identify anything that may have an immediate impact on your health, we would inform your GP about the nature of the problem and about who you are. The routine referral procedures applicable in the NHS would then be used to get in touch with you and provide advice. If you wish, we will send you a copy of the final publication on the overall outcome of our study as and when this is available – please let us know so that we can make a note of that.

Who is organising and funding this study?

The research is organised through Dr. Andreas Goebel, a consultant doctor with expertise in treating patients with chronic pain, who is working in an NHS Trust in the UK, and through scientists and doctors interested in the immune system and pain. The University of Liverpool is sponsoring and coordinating this study. The University of Liverpool holds insurance with Griffiths & Armour that covers the management and design of this study.

Funding is provided by the Pain Research Institute, associated with the University of Liverpool, and the Pain Relief Foundation, a registered UK charity. Funders have no further say in the conduct of the study.

Who do I contact if I want to take part in the study, have any further questions or any concerns?

In order to register your interest in taking part in the ABPP study, or if you have any questions or concerns, please use the contact details below:

Hayley McCullough
Pain Research Institute Administrator
Email: Hayley.Mccullough@liverpool.ac.uk
Telephone: 0151-529-5835

Normal working hours Monday, Tuesday and Friday 8am-2pm
**Please be aware, times may change due to COVID-19*