The Story Behind Cognitive Impairment and Lupus Brain Fog Webinar

Questions from Participants:

1. Movement Dysfunction, would that include vertigo? How would one go about making that go away?

The motor aspects mentioned in our talks, such as manual motor speed and dexterity are one of the cognitive domains. This domain reflects your ability to perform several tasks that involve hands and coordination and is different to vertigo and movement dysfunction.

Vertigo doesn't fall under the umbrella of cognitive dysfunction but could be related to problems in the inner ear or stroke/brain. This is something that would always need to be discussed with your primary care physician.

2. Can one get any of these dysfunctions even if your lupus is in remission?

Unfortunately, yes. Cognitive impairment (CI) can be attributed to active lupus but this is not the only cause. Other causes can include depression, fatigue, sleep disturbance, pain and certain medications.

3. what is the age range of participants in your study and sample size?

There were several studies mentioned. The age range tended to be 18-70 years old with an average of early 40s.Depending on the study participant number varied, for example the brain imaging studies had 56 participants with SLE, the systematic review of CI prevalence in SLE had 2463 patients with SLE from 35 different studies and the study looking at different measures of CI in SLE had 211 patients with SLE.

4. how does ACR testing differ from MOCA or MMSE in measuring CI? I work in primary care and I've only used Moca and mmse.

The MoCA and MMSE are what we call "screening measures". They are quick to administer and are able to show if someone has cognitive impairment. Originally they were designed for identifying dementia which is very different to the impairment we see in SLE. These measures still need to be validated in lupus and further research is needed to ensure they are appropriate for looking at CI in lupus.

The ACR neuropsychological battery is longer and has many different measures. It looks at different types of cognition (e.g. learning, memory, planning, attention, verbal and spatial issues). It can identify which type of cognitive problem the participant has. It can also pick up on more subtle changes and give a better understanding of the impact on daily life. It is a better measure for CI in SLE but requires a trained professional to administer it and has higher cost implications.

5. Can common SLE therapies (biologics, immunosuppressants or steroids) impact biomarkers considered in measurement/testing for CI? Further to that, will Lupus therapies improve CI?

It is very important to know which CI you are dealing with. If you remember from our presentation we highlighted the difference between CI and brain fog and we believe that the treatment may need to be different too.

It is still unclear as to what effect common SLE therapies have on CI. Research suggests that an increase in inflammation and/or active disease negatively affects CI. Therefore, by treating the active disease there is a possibility that the CI might improve.

However, the effects of SLE therapies on CI when a patient does not have active disease are less certain. Depending on the treatment there have been suggestions of improvement, no change and a temporary negative effect.

There are studies that are just about to start using other therapies that may help with CI in SLE and this is also something that we are hoping to look at in the future.

6. how do we know that we got brain fog rather than CI?

In our talk we suggested that brain fog and CI are two different concepts. We suggested that brain fog is cognitive fatigue possibly due to overuse of your brain. A feeling that you can't think or concentrate or do things as well/quickly as you once did. However, you do still manage to do things. Often, by developing coping and adaptive approaches to better handle the tasks you are doing. As such, when formally tested you would be found to have adequate levels of cognitive function but may experience a "fogginess".

We defined CI as performing badly on formal cognitive tests and struggling more on daily tasks.

As such, there are two ways of measuring cognition. One way is by a healthcare team using objective standardised tools and the second way is to get feedback from patients on their own symptoms, using patient reported outcomes. Both are very important.

Brain fog and CI are very much linked and we are looking to see how to differentiate each aspect. We are also looking to see if brain fog leads onto CI and in what situation this may happen.

7. Is there a specific auto-antibody that is common in individuals that have CI?

Unfortunately, there is not one clear auto-antibody common in individuals with CI. Studies have shown a few that may be involved but it does not mean if you have this auto-antibody that you have CI. Some of the auto-antibodies that have been associated with CI in SLE are:

- Anti-phospholipid
- Anti-ribosomal P
- Anti-N-methyl-D-asparate
- Anti-dsDNA

CI would suggest changes within the brain. Unlike the other organs within the body there is a barrier to the brain which can protect it from auto-antibodies within the blood. This is good news, but it does mean that measuring blood samples and auto-antibodies only, doesn't give us enough information to determine their effects on CI in SLE.

8. Is this studying published in any medical journals? It would be great to share this information with various medical teams.

Yes, the research mentioned is published, please see the following links:

- Cognitive Function Trajectories in Association With the Depressive Symptoms Trajectories in Systemic Lupus Erythematosus Over Time: https://onlinelibrary.wiley.com/doi/10.1002/acr.24349
- What is the prevalence of cognitive impairment in lupus and which instruments are used to measure it? A systematic review and meta-analysis: https://www.sciencedirect.com/science/article/pii/S0049017217305826?via%3Dihub
- Metrics and definitions used in the assessment of cognitive impairment in systemic lupus erythematosus: A systematic review: https://www.sciencedirect.com/science/article/pii/S0049017221001104?via%3Dihub
- Validity Evidence for the Use of Automated Neuropsychologic Assessment Metrics As a Screening Tool for Cognitive Impairment in Systemic Lupus Erythematosus: https://onlinelibrary.wiley.com/doi/10.1002/acr.24096
- Altered cognitive function in systemic lupus erythematosus and associations with inflammation and functional and structural brain changes: https://ard.bmj.com/content/78/7/934.long
- Cognitive dysfunction and functional magnetic resonance imaging in systemic lupus erythematosus: https://journals.sagepub.com/doi/10.1177/0961203315593819?url_ver=Z39.88-2003&rfr_id=ori:rid:crossref.org&rfr_dat=cr_pub%20%200pubmed

- The effects of disease activity on neuronal and behavioural cognitive processes in systemic lupus erythematosus: https://academic.oup.com/rheumatology/advance-article/doi/10.1093/rheumatology/keab256/6184875

9 Is there a link between CI and APS with history of ~12 TIA's within 5 month period?

Yes, unfortunately having APS, stroke, TIA do give a higher risk of CI.

10. does one have to have active lupus as shown on blood tests to be able to attribute any cognitive impairment to lupus? in other words, if lupus is under control and cognitive issues are experienced, should other causes be sought, or could lupus be causing them, in the absence of any other active lupus?

These are good questions and ones that we are trying to understand better. In answer to your initial question - no, you do not have to have active lupus (as shown from blood tests) to have your CI attributed to SLE. Active lupus is just one of many factors that could be causing CI in lupus patients. The CI may be caused by conditions other than lupus activity such as depression, poor sleep quality, fatigue, pain, brain changes and certain medications. All these can be a consequence of lupus or additional conditions. It is important that all potential causes are looked at to better determine an appropriate treatment. This is something that we are working towards.