Sample information for studies involving Transcranial Ultrasound Stimulation (TUS)

What is TUS?

Low-intensity focused ***transcranial ultrasound stimulation (TUS)*** is a technique that uses ultrasound waves to produce a temporary and reversible change in brain activity in a specific target region. Using TUS, we can safely and non-invasively modulate brain activity by delivering pulses of ultrasound waves with a transducer placed over the head.

What happens during the TUS session?

During the ***TUS procedure***, we will position a transducer over your scalp, in contact with your head. To position the TUS correctly, we will use some gel to allow good contact with the transducer. Once the transducer is positioned correctly, pulses of ultrasound are used to modulate the brain. The TUS produces a very small sound when active but it is barely audible so you may not hear it. We will tell you when we deliver the stimulation. <*This will be very brief, less than 2 minutes per area.*> We will follow the guidelines of the Food and Drug Administration (FDA) and the TUS parameter limits prescribed for neuromodulation (see below for more details on safety).

At the ***end of the session***, you will be provided with a towel and shampoo to wash the gel from the TUS off your hair before leaving the BRIC. You may wish to bring a comb and your own hair products if you prefer.

We will ask you to complete a side effects questionnaire for the TUS stimulation at the end of each study visit. We would appreciate if we could contact you again 1 month after the session to ask you to complete the same questions again, although this is optional.

What are the risks of taking part in this study?

TUS is non-invasive and safe; you should not experience long-lasting discomfort or side effects.

The FDA regulates ultrasound exposure for neuromodulation. The safety limits for exposure are similar to those used for obstetric diagnostic ultrasound and adult cephalic applications. It is noteworthy that, in the four decades that it has been in use, diagnostic ultrasound has produced no harm to participants. However, the parameters used for TUS are different from the ones used for diagnosis. While diagnostic ultrasound comprises brief pulses of higher frequency (in the MHz range), TUS typically rests on longer pulses at lower frequencies (in the sub-MHz range). These two parameters (duration and frequencies) are regulated by FDA guidelines. We will follow these regulations carefully.

A recent safety study (Legon, 2020) gathered data from multiple human TUS studies (more than 200 participants). The data to date shows that TUS is safe for neuromodulation. Side effects are similar to those reported in response to other forms of non-invasive neuromodulation (like TMS or tES). For example, participants may experience some

discomfort during TUS. In susceptible individuals, TUS may cause headache, which usually responds well to over-the-counter painkillers (e.g. paracetamol).

The amount of ultrasound exposure at experimental strength (i.e. applied directly to the brain) will also be limited to a cumulative maximum of 16 minutes of pulsed TUS stimulation per 8 weeks (1 session of 2min maximum every week) and a maximum of 8 sessions of stimulation over 12 months. This will be determined by means of experimental records in the form of a screening questionnaire, upon which the cumulative stimulation will be listed. Forms will be kept in a lockable cabinet in Dr Fouragnan's office.

Risk of seizure: TUS has a very high spatial accuracy with a region of 90%-maximum intensity that does not exceed a few millimetres shaped in an ellipse form. In addition, there is variability in neuronal responses to TUS. This prevents the possibility of large-scale neuronal firing compared to other forms of stimulation such as transcranial magnetic stimulation where the spatial distribution extends to several centimetres in some directions. **Thus, TUS will not cause seizures.** In addition, there has been no report of seizures in more than 10 human studies and more than 30 animal studies (Pasquinelli et al., 2019; Legon, 2020). However, as a precaution, we will not give TUS to someone with a personal or close family (e.g., parent, sibling, or child) history of epilepsy, another significant neurological or psychiatric disorder, or extreme mood fluctuations. If you are taking any medication or suffer from migraine headaches, you should discuss this with the researcher beforehand.

It is our policy not to give TUS to someone who is pregnant. Therefore, if there is a possibility that you are pregnant, you must not take part in this study.