Project Description / Protocol

1. Project Title

- **PTSD Clinic Research Project: Examining the biopsychosocial predictors of treatment response to propranolol-based reconsolidation therapy for trauma- and stressor-related (TSR) disorders.**
- Version number: 2.1

2. Project Team Roles & Responsibilities

Principal Investigators

Professor Alain Brunet (Director of the National PTSD Research Centre at UniSC's Thompson Institute [TI/NPRC]). Alain Brunet has investigated the impact of trauma exposure on individuals for more than 20 years, with a special focus on characterising psychosocial and biological risk and resilience factors in posttraumatic stress disorder (PTSD). Professor Brunet has developed a novel treatment called Reconsolidation Therapy (RT) which has been used with victims of terrorism in the Bataclan (Paris, France). The development of this treatment earned him several awards. Professor Brunet is also past co-editor of the Journal of Traumatic Stress, the premier specialty journal in the field of traumatic stress, and vice-president of the International Society for Traumatic Stress Studies.

Professor Brunet has been a select member of the Canadian Academy of Health Sciences since 2021. In 2022, he won the career award of the Canadian Psychological Association – Traumatic Stress Section. In 2023, he won the Leo-Pariseau Award which annually recognizes the excellence and influence of an individual's work in the field of biological or health sciences in French Canada. His expertise in TSR disorders ranks among the top 1% in the world according to www.expertscape.com, and he has an H-index (scientific publications impact) of 56. Professor Brunet is a registered clinical psychologist in Québec, Canada. **Role**: Alain Brunet will lead the research program of the clinic, including overseeing the implementation of the study protocols, managing study timelines, overseeing the dissemination of results, and providing mentorship to the Clinical Programs Manager and team.

Dr Chris Moller (General Practitioner). Dr. Chris Moller has been a practicing medical doctor for 14 years of in clinical practice and served as a full time Military Medical Officer for 5 years, and as a Military Reservist for a further 5 years. Dr. Moller has been a Principal Investigator on 9 clinical studies and a sub-investigator on 11 others. He brings expertise in clinical research, generalised medicine, medical management of mental health conditions, and military medicine, with a focus on rigorous trial design, regulatory compliance, and patient safety.

His research experience includes working as a Research Medical Officer at the Australian Defence Force Malaria and Infectious Diseases Institute, where he participated in epidemiological investigations and clinical trials aimed at improving force health protection, and the University of the Sunshine Coast clinical trials centre where he was principal investigator for a number of sponsor-led inpatient and outpatient studies including vaccine trials, medical device trials, and first-in human studies. **Role:** Dr Moller will be responsible for conducting all medical evaluations, including comprehensive physical health assessments to determine participant eligibility and safety for study inclusion. This role involves reviewing medical histories, identifying any contraindications to study medications, and assessing for comorbid conditions that may impact treatment outcomes. Dr Moller will also oversee the prescribing of study medications, closely monitor participant responses, and evaluate for any adverse effects throughout the trial. Additionally, he will communicate and collaborate with the research team and community healthcare providers to ensure continuity of care, facilitate appropriate referrals, and address any emerging medical concerns.

PTSD Clinic Director (TBA) - Currently being recruited.

Co-Investigators

Trish Wilson (PTSD Clinic Manager, & Clinical Programs Manager). Trish Wilson is a nurse registered with the Australian Health Practitioner Regulation Agency (AHPRA), with significant experience in managing diverse multi-disciplinary teams within the community setting. At the TI/NPRC, she oversees clinical management of the staff working in the Clinical Research Unit and the teams providing clinical programs including EMERALD, a well-being and lifestyle focused mental health program, ENGAGE and EMERGE both research programs for supporting

people and building resilience for people affected by extreme weather events, disruption and other traumatic experiences. **Role**: Trish will play a key role in the oversight and implementation of the research program. This will involve ongoing management of the program and staff, meeting of timelines and budgets, and the co-ordination of community engagements.

PTSD Mental Health Clinicians/Research Therapists (TBA) - Currently being recruited.

Dr Bonnie Quigley (Molecular Biology program leader). Bonnie Quigley is the current program lead for Molecular Biology at the TI/NPRC and manages the molecular biology (PC2) research laboratory. Classically trained as a microbiologist and immunologist, Bonnie has 16 years of post-PhD experience undertaking and leading molecular biology research projects internationally in both the public and private sector. Bonnie has a track record in the microbiology/molecular biology space of 73 publications (with an h-index of 33), giving her extensive experience in translating research data into significant publication outputs. **Role:** Bonnie will oversee and manage the molecular biology sample collection, testing and analysis related to the project.

Dr Jacob Levenstein (Research Fellow – Neuroimaging). Jacob Levenstein is a Research Fellow in Neuroimaging at UniSC's TI/NPRC with broad interests that include neurophysiology, neuropsychology and brain stimulation. Since 2012, he has been involved in brain imaging research, working across several world-leading neuroimaging institutes. Jacob completed his DPhil at the University of Oxford within the Wellcome Centre for Integrative Neuroimaging (WIN/FMRIB). In 2016, he was awarded a five-year National Institutes of Health Oxford-Cambridge Scholar Fellowship. Jacob was trained as an MRI Research Technician at Massachusetts General Hospital/Athinoula A. Martinos Center for Biomedical Imaging, where he applied several MRI modalities to measure the human motor system in healthy participants and those affected by movement disorders. **Role**: Jacob will oversee and manage the neuroimaging collection and analysis related to the project.

Fiona Randall (Registered Nurse, Quality and Risk Coordinator). Fiona Randall is an AHPRA registered nurse who has worked across multiple settings including clinical research, hospital health services, aged care, community health, public health, and education. Fiona has expertise in the development and delivery of healthcare education, policy development, health service project management, translating research into clinical practice, and clinical quality and patient safety. Fiona's research interests include nursing, infection prevention and control, education, and organisational psychology. At the TI/NPRC Fiona's work as the Quality and Risk Coordinator focuses on ensuring that clinical services, research processes, and data collection adhere to quality standards and protocols. **Role**: Fiona will be responsible for ensuring that all aspects of the research study are conducted in accordance with ethical guidelines, regulatory standards, and institutional policies. By maintaining a high standard of compliance and safety, this role safeguards the integrity of the research and the wellbeing of all participants.

Kara Huggins (Clinical Administration Officer). Kara Huggins is the current Clinical Administration Officer for the Myndset, EMERALD and ENGAGE programs at the TI/NPRC. She has 30 plus years' experience in administration with over 7 years of high-level administration in clinical settings. Kara's strengths lie in her systematic approach and her attention to detail, striving for better workflows, leading to better outcomes for colleagues, clients and the wider community. **Role**: Kara plays a pivotal role in ensuring the smooth operation of our research study. Kara will oversee the coordination of participant recruitment, data collection, scheduling of appointments, and maintenance of accurate records.

Monique Jones (Registered Nurse). Monique Jones is an AHPRA registered nurse has worked in mental health since graduating as a Registered Nurse in 1997 at Ara in Christchurch, New Zealand. She has two Postgraduate Diplomas in Health Science endorsed in Mental Health and endorsed in Cognitive Behaviour Therapy from Otago University. Her clinical experience includes working with children and adolescents as well as adults in inpatient settings, working with adults with problematic anxiety in a specialist community service in New Zealand. Once moving to Australia, she has worked with adults with depression, anxiety, addiction and post-traumatic stress in both inpatient and outpatient settings. Prior to her current role as a clinic coordinator, Monique worked in the clinical trials unit at the TI/NPRC. **Role**: Monique will conduct telehealth screening sessions to monitor participant eligibility and wellbeing both prior to the start of the treatment and following the conclusion of the intervention. She will be responsible for collecting clinical data, assessing any adverse events, and ensuring adherence to the

study protocol during these interactions. Monique will also act as a liaison between the research team and participants, providing support and clarifying study-related information as needed.

3. Resources, Support and Other Approvals

3.1 Funding

This project is an investigator-lead, internally funded study, supported by philanthropic funds.

3.2 Project Resources and Context

The study will be conducted in the PTSD Research Clinic at the TI/NPRC. All needed resources to conduct the study are provided within the Institute. The Clinic is a research facility offering treatments at no cost in exchange for participation in leading edge research. This clinic is designed to help us to uncover the best ways of treating TSR conditions like PTSD as well as help us understand how to reduce the incidence of comorbid conditions.

This research study is the first project run out of the PTSD Research Clinic, marking the beginning of a larger research program dedicated to exploring emerging treatments for PTSD and other trauma-related conditions. The clinic will soon be offering multiple research studies aimed at understanding and improving treatment options for individuals affected by stress and trauma. Potential participants will be carefully triaged into the most suitable clinical pathway following a comprehensive assessment to ensure they receive the best support and intervention. For those not eligible for the studies, appropriate referrals will be made to local clinical services to ensure continuity of care and access to alternative treatment options.

4. Background

4.1 Impact of Trauma

The global prevalence of trauma exposure is high, with research consistently indicating that a significant majority of individuals have experienced trauma in their lifetime (Douglas et al., 2023). The World Health Organisation found that 70.4% of adults had experienced at least one traumatic event in their life (*N* = 70,000, 24 countries) (Kessler et al., 2017). The now infamous Kaiser Permanente's and Centre for Disease Control's Adverse Childhood Experiences study found that 64% of people had experienced at least one adverse event and 12% had experienced four or more before 18 years old (Felitti et al., 1998). More recently, the Australian Child Maltreatment Study found that many Australians have experienced child maltreatment, including physical (32%), sexual (28.5%), and emotional (30.9%) abuse and exposure to domestic violence (39.6%) (Matthews et al., 2023).

Cumulative trauma can exhaust the body's stress response, damage developing brains' functions and structures, and lead to performance deficits across multiple areas including: behavioural and emotional dysregulation, learning, attention, and language use, difficulty navigating relationships, poor decision making, and dysfunction in fear extinction (Evans & Coccoma, 2014, Kisiel et al., 2014, Sheridan et al., 2020, Van der Kolk et al., 2005). The extensive body of evidence documenting the adverse effects of trauma on childhood development and its lingering impact on our physical and psychological health as adults has been a catalyst for significant advances in how we support individuals who have experienced a traumatic event. It has also deepened our understanding of a major psychological consequence that can emerge from such experiences: PTSD.

Post-Traumatic Stress Disorder (PTSD)

PTSD is a possible outcome of exposure to a traumatic event. Individuals who have a PTSD diagnosis may recurrently experience memories, emotions, and sensations of a traumatic event through sensory nightmares or flashbacks, have difficulty sleeping, poor concentration, hypervigilance, irritability, emotional withdrawal and experience avoidance (Yehuda et al., 2015). PTSD related nightmares have been linked with a five-fold increase in suicidality and can be resistant to treatment (Sjostrom et al., 2007).

A wide variety of traumatic events can cause PTSD (Kessler et al., 2014; Yehuda, 2002), and the specific type of traumatic event can influence the course of the disorder (e.g., chronic vs non-chronic, immediate vs delayed onset) (Santiago et al., 2013; Smid et al., 2009). Taking this into account, it has been estimated that 11% of

Australians will experience PTSD at some point in their life, with women being at almost twice the risk of men (14% and 8% respectively) (ABS, 2022).

Typical PTSD treatment may involve the use of pharmacotherapy, psychological therapy, or a combination of both. Clinical guidelines recommend sertraline, fluoxetine, paroxetine, and venlafaxine as pharmacologic treatments for PTSD, despite evidence demonstrating only marginal efficacy over placebo (Hamblen et al., 2019; Martin et al 2021; Hoskins et al; 2021).

Trauma-focused psychotherapies (TFPs) are among the most supported treatments for PTSD, demonstrating greater effect sizes compared to current pharmacological options (Mavranezouli et al., 2020; Weber et al., 2021). TFPs are based on the premise that by facilitating emotional regulation while an individual is being exposed to their trauma memory will result in extinction learning, altering trauma related cognitions, and reducing avoidant behaviours. Prolonged Exposure (PE), Cognitive Processing Therapy (CPT), Trauma-focused Cognitive Behavioural Therapy (TF-CBT), and Eye Movement Desensitisation and Reprocessing (EMDR) are recommended treatments for adults while TF-CBT or EMDR are commonly suggested for children and adolescents (Hamblen et al., 2019; Martin et al., 2021, APA, 2017; NICE, 2018, Lewey et al., 2018, Lewis et al., 2020, McLean et al., 2022).

Whilst TFPs have shown the most robust effect sizes of all currently accepted PTSD treatments, treating PTSD in clinical practice remains fraught with difficulties. TFPs are usually delivered over 8-16 weeks (Watkins et al., 2018) by highly trained specialists. It is marked by high drop-out rates, high risk of relapse, treatment resistance, and significant residual symptoms (Tripp et al., 2020; Larsen et al., 2019; Smid et al., 2018; Niles et al., 2018; Green, 2013). Similarly, the modest outcomes of pharmacological treatments over placebo often do not justify the associated costs, impact of long-term use, and adverse side-effects individuals may experience. As a result, new approaches are needed to enhance treatment efficacy and provide lasting relief from trauma symptoms.

Memory Reconsolidation Blockade: An Emerging Trauma Treatment

The concept of memory reconsolidation blockade has been proposed as a potentially more effective method than extinction training (Nader & Hardt, 2009). A landmark study by Nader et al. (2000) showed that administering a protein synthesis inhibitor (anisomycin), following the reactivation of a fear memory could block (or impair) the reconsolidation of that memory in rodents. Subsequent studies in humans have shown that the reconsolidation of emotional memories can also be disrupted when specific pharmacological agents are used alongside the recall of traumatic events (Bergstrom et al., 2013, Parsons and Ressler, 2013, Ratano et al., 2014; Kindt et al., 2009).

The most used pharmacological agent in reconsolidation blockade research involving humans is propranolol. Propranolol is a lipophilic nonselective β-adrenergic receptor (β-AR) antagonist that crosses the blood-brain barrier, impacting the noradrenergic system and, putatively, the protein synthesis process (Przybyslawski et al., 1999; Cahill et al., 2000, O'Carroll et al., 1999). It has been widely employed in the treatment of conditions such as hypertension, ischemic heart disease, and arrhythmia (Srinivasan, 2019).

In preclinical studies, propranolol has consistently blocked the reconsolidation of fear memories across various tasks involving memory, including passive avoidance, contextual fear, and auditory fear conditioning (Debiec & Ledoux, 2004; Przybyslawski et al., 1999; Taherian et al., 2014). In humans, Cahill and colleagues (2000) demonstrated that, compared to a placebo, oral propranolol administered before viewing emotionally disturbing slides prevented the heightened emotional recall of those images. In patients, a randomised controlled trial by Brunet and colleagues (2018) found that oral propranolol was associated with reduced PTSD symptoms after six sessions, during which patients recalled a traumatic event 90 minutes after taking propranolol. Furthermore, propranolol has been shown to disrupt fear memories in healthy individuals (e.g., Kindt et al., 2009). It has also led to significant improvements in PTSD, anxiety and depression symptoms by the end of treatment in children exposed to war-related trauma in an open-label trial (Thierree et al., 2020).

Of four meta-analyses, two support reconsolidation impairment (Lonergan et al, 2013; Pigeon et al, 2022) and two others consider that the evidence is inconclusive (Raut et al., 2022; Steenen et al., 2022). Raut et al. (2022) meta-analysis examining oral propranolol interventions for disrupting trauma memories in PTSD patients reviewed seven studies reporting PTSD symptom changes and three studies assessing propranolol's effects on physiological responses. Interestingly, the findings indicated that propranolol did not significantly improve PTSD

symptoms, skin conductance, or electromyography responses, though it did reduce heart rate following trauma memory recall vs. placebo. However, there were methodological limitations across the studies, such as inconsistent propranolol dosages, variations in treatment session protocols, small sample sizes, and heterogeneity in effect sizes (Raut et al., 2022). This suggests that there are probably boundary conditions (some that have yet to be discovered) governing the use of reconsolidation impairment as a therapeutic modality. As a result, the authors recommended interpreting these findings with caution and called for more research on the topic.

Given the immense and growing burden of TSR conditions, which poses a significant crisis for individuals and public health systems, current therapeutic options alone are insufficient to address the problem. While the efficacy of propranolol-based reconsolidation blockade for patients remains under debate, the model is based on a strong animal model and emerging evidence suggests that it holds significant promise as a clinical treatment for TSR disorders, opening the door to therapeutic innovation. This potential lies in the unique attributes of reconsolidation blockade, which, unlike traditional PTSD treatments, offers the possibility of shorter therapist training, shorter treatment durations, low cost, good treatment acceptability, reduced adverse side effects, and reduced reliance on intensive clinical expertise. Thus, this research proposal aims to build on the existing literature to further investigate the usefulness of reconsolidation blockade as a therapeutic modality. By exploring this approach, we seek to expand on the potential benefits of targeting memory reconsolidation as a means of providing more effective and accessible treatment for individuals suffering from TSR disorders.

4.2 Aims

Primary aim: To determine if a 6-session course of reconsolidation blockade (i.e., oral propranolol treatment combined with script-driven trauma recall) is efficacious in reducing PTSD symptom frequency and severity in adults.

Exploratory aims: To examine the psychosocial, neurocognitive, neurobiological, neuroimaging and physiological effects of reconsolidation blockade treatment in adult participants with PTSD.

4.3 Research Questions

1. Primary question: Will a 6-session reconsolidation blockade treatment be efficacious in reducing core PTSD symptoms frequency and severity.
2. Secondary question: Are there psycho-social, cognitive, and biological markers (genetic, circulating, and neural) that can predict treatment response to reconsolidation blockade treatment?

5. Project Design

	Screen	**T1 Baseline Week 0**	**T2 Pre-treatment (after 4-week waitlist)**	**Intervention Weeks 1–6**	**T3 Post-treatment Week 7 or 8**	**T4 Follow up 1 1-month**	**T5 Follow up 2 3-month**
Research Activity	30-min phone call	4-hour clinical assessment: Medical ax* Psycho-diagnostic ax Heart rate variability Substances screen Self-report measures - PDI - PDEQ - PCL-5 - IES-R - BDI-I - PTGI	4-hour clinical assessment: MRI CANTAB Biological ax Hair Clip Self-report measures -PCL-5 -IES-R -BDI-I - Any sig. changes from T1?	50-min RT session in week 1 Thereafter once weekly 25-minute RT sessions in weeks 2-6 Saliva IES-R	4-hour clinical assessment: MRI CANTAB Psych interview Biological ax Self-report measures - PCL-5 - IES-R - BDI-I - WHOQOL - PSQI	50-min clinical interview Self-report measures -PCL-5 -IES-R -BDI-I	4-hour clinical assessment: MRI CANTAB Psych interview Biological ax Hair clip Heart rate variability Substances screen Self-report measures -PCL-5 -IES-R -BDI-I -PTGI

		- ITQ - CTQ - WHOQOL - PSQI Eligibility met/not met					-WHOQOL - PSQI
Setting	Tele-health	UniSC	UniSC	UniSC	UniSC	Telehealth	UniSC
Participants	>18yro Diagnosed PTSD	>18yro Diagnosed PTSD	>18yro Diagnosed PTSD	>18yro Diagnosed PTSD	>18yro Diagnosed PTSD	>18yro Diagnosed PTSD	>18yro Diagnosed PTSD
Identifiability during data collection	Identifiable	Identifiable	Identifiable	Identifiable	Identifiable	Identifiable	Identifiable
Identifiability during data storage	Re-identifiable	Re-identifiable	Re-identifiable	Re-identifiable	Re-identifiable	Re-identifiable	Re-identifiable
Identifiability at the time of publications	Non-identifiable	Non-identifiable	Non-identifiable	Non-identifiable	Non-identifiable	Non-identifiable	Non-identifiable
Recruiting methods	-Social media -Flyers -Website -Email circulated to referral networks	n/a	n/a	n/a	n/a	n/a	Email/phone call to previous participants who consented to future contact
Consent	Verbal via survey question	Written Unspecified Written consent requested to contact for future projects	Verbal	Verbal	Verbal	Verbal	Verbal
Risks and Benefits	-Distress -Discomfort	-Distress -Discomfort	-Distress -Discomfort -Side effects re: blood draw and imaging session	-Distress -Discomfort -Reduced PTSD symptoms -Adverse effects from study medication	-Distress -Discomfort -Reduced PTSD symptoms -Side effects re: blood draw and imaging session	-Distress -Discomfort -Reduced PTSD symptoms	-Distress -Discomfort -Reduced PTSD symptoms -Side effects re: blood draw and imaging session
Data Storage	Downloaded from Qualtrics, stored on R drive	R drive Consent forms – locked filing cabinets	R drive Consent forms – locked filing cabinets	R drive Consent forms – locked filing cabinets	R drive Consent forms – locked filing cabinets	R drive Consent forms – locked filing cabinets	R drive Consent forms – locked filing cabinets
Results/ Outcomes/ Future	Publication Future related projects	Publication Future related projects	Publication Future related projects	Publication Future related projects	Publication Future related projects	Publication Future related projects	Publication Future related projects

*ax = assessment

5.1 Methodological Approach

In this study, participants will receive manualised (Brunet & Lonergan, 2010) propranolol-based reconsolidation blockade treatment (hereafter called RT) once per week for six weeks in a single treatment arm. Each RT session will be conducted by trained practitioners. Session 1 will last 50 minutes while Sessions 2-6 will last 25 minutes and involve a script recall exercise to activate the specific trauma memory targeted for that session. Participants will be instructed to take the study oral medication (1mg/kg according to ideal weight) 60 minutes with a light snack before each scheduled RT session (i.e., 6 once-a-week doses over 6 weeks). The first dose will be taken on site under supervision of a registered nurse with access to a medical doctor. Subsequent doses will be taken at home before each treatment session. On the day of the first propranolol administration, the research trials

physician (GP) will be on-site to monitor for potential hypotensive events and ensure participant safety. This protocol builds on previous propranolol research and aligns with memory reconsolidation theory principles.

Throughout the study, participants will remain under the care of their existing treating team (i.e. medical practitioner, psychiatrist and/or psychologist), who will oversee any modifications to their existing treatments. RT will be used as an adjunctive treatment, allowing participants to maintain their current psychotropic medications, if any, under their physician's guidance. Any changes in medication will be documented by the study staff. It will be strongly recommended to participants and their treating team to not commence any new mental health treatments during the clinical study.

The primary outcome of the study is a change in PTSD symptomatology, assessed using the battery of psychological assessments (i.e., PCL-5, structured clinical interview) at several time points:

- T1 Baseline assessment (week 0)
- T3 post-treatment assessment (week 7 or 8)
- T5 Follow-up 2 (3 month)

5.2 Participants

Male and female adult participants aged 18 years and older, with a current diagnosis of non-complex PTSD, as assessed using the battery of tests within our psychological assessment protocol. The study will aim to recruit 150 participants. Investigators will keep a record of participants who were considered for the study but were not enrolled. This is done primarily to document the selection process, ensure transparency, and identify any potential selection biases. Please refer to section 5.3 for the process involved with the Participation Screening and Identification Log. Participants with a condition that may contraindicate the use of MRI will still be eligible to take part in the overall study. Only participants who meet all of the inclusion criteria and none of the exclusion criteria will be eligible to participate in the study.

Inclusion criteria:

- Persons aged 18 years +
- Participants must be able to understand Research Project Information Sheet (RPIS) and provide written informed consent on the Participant Informed Consent Form (PICF) (including both adequate intellectual capacity and fluency in English language)
- Diagnosis of PTSD
- Participants must undertake psychological, cognitive, and biological assessments, tolerate propranolol and not be taking any drugs that could contraindicate propranolol.
- Participants must have a current treating team who is managing their mental health diagnosis
- Persons of child-bearing potential must agree to use a *highly effective method of contraception

*Highly effective methods of contraception are listed below:

  - Hormonal methods of contraception including oral contraceptives containing combined estrogen and progesterone, a vaginal ring, injectable and implantable hormonal contraceptives, intrauterine hormone-releasing system (e.g. Mirena) and progestogen-only hormonal contraception associated with inhibition of ovulation o Nonhormonal intrauterine device (IUD)
  - Bilateral tubal occlusion
  - Vasectomised participant/partner with documented azoospermia 90 days after procedure, if that partner is the sole sexual partner.
  - Abstinence from heterosexual intercourse: when this is in line with the preferred and usual lifestyle of the participant.

Periodic abstinence (e.g., calendar, ovulation, post-ovulation methods) and withdrawal are not acceptable methods of contraception. Persons in the following categories are not considered persons of childbearing potential

- Person without a uterus
- Premenarchal

- Premenopausal with permanent infertility due to 1 of the following:
    - Documented hysterectomy
    - Documented bilateral salpingectomy
    - Documented bilateral oophorectomy
- Postmenopausal - A postmenopausal state is defined as no menses for 12 months without an alternative medical cause

Exclusion criteria:

- Complex PTSD
- Significant psychiatric condition: psychosis, bipolar disorder, personality disorder, substance use disorder
- Any contraindication to propranolol as determined by the study physician
- Development of serious, adverse, or unexpected events/reactions during the trial
- Previous allergy or reaction to propranolol, or other beta-adrenergic blocking agent
- Participation in any other clinical study at the time of enrolment, or having received any investigation product within 30 days of the day of enrolment onto the study
- Currently pregnant, breastfeeding or intending to become pregnant during the course of the study.
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- Any other condition that, in the opinion of the investigator, may adversely impact the safety of the participant or the accuracy of the study data

5.3 Recruitment and Consent

The study is scheduled to begin in November 2024, with the inclusion of the first 'pilot' participant. Data collection and analysis will continue throughout the study and the study endpoint is December 2027. Participants in the pilot will be recruited from contacts in our Realtime Database who have already expressed interest in participating in trauma-related clinical trials. Additional advertising for the research project will be undertaken by the TI/NPRC engagement and marketing team and will include direct emails sent to our established community partnerships. Recruitment will also occur online using approved advertisements and flyers on the TI/NPRC website and social media platforms such as Facebook. Additionally, participants may be recruited through public information sessions and forums organised by the TI/NPRC, both on and off-site, as well as through the Primary Health Network. Local healthcare professionals, such as general practitioners, specialists, medical officers, psychiatrists, and psychologists, will be informed about the study to facilitate referrals.

See Appendix C for a visual journey of the pathway through the program. Each participant is required to have a general practitioner (GP) or specialist referral prior to being included in this study who will continue to manage the participants' mental health during the trial period. We will send the referring GP or specialist a letter detailing the participants' participation and outcomes of the trial upon completion of the study. If potential participants are referred by practitioners other than a GP or psychiatrist, we will ask them to obtain an appropriate referral from a GP or psychiatrist before including them in the study.

Every participant who is identified as potentially suitable for enrolment into the study will be entered into a Participant Screening and Identification Log. Information on the log will include the participant's initials, participant's date of birth, screening number, screening outcome (with a reason if found to be ineligible) and whether they are eligible to be rescreened with the approximate rescreen date recorded.

All potential participants will receive a digital version of the Research Project Information Statement (RPIS) via email prior to screening and the RPIS and consent form (Appendix A and B) via email prior to baseline (T1). The RPIS will detail the study process, including the assessment, intervention sessions, and data collection timeline.

Participants will be informed that their participation in the study is entirely voluntary. Only after reviewing the RPIS will participants have the option to provide their written consent. Participants will be encouraged to involve their treating doctor, family members, carers, and/or a support person when deciding whether they would like to participate or not. A support person can be present with participants during the research study to provide assistance and comfort as needed. If participants choose not to participate, they will be offered alternative

community service options. Participants will provide verbal consent before the following time points (screening, T2, treatment appointments, T3, T4, T5).

We will be seeking unspecified consent for the collection and future use of their data. This approach allows for the responsible and ethical use of collected information beyond the scope of the current research, supporting future studies in the field of mental health. Given the broad and evolving nature of mental health research, it is essential to have access to high-quality, ethically obtained data that can be used to answer new research questions as they arise. By consenting to unspecified future use, participants contribute to a legacy of mental health knowledge, aiding in the development of more comprehensive treatment approaches and contributing to the overall understanding of mental health conditions. Please refer to the informed consent operating procedure (Appendix N) for more detail on the consent process. All potential participants will be informed on their ability to withdraw from the study at any time.

We will incorporate an optional consent process for specific elements, including leftover biospecimens, video recordings, and contact details for future follow up. We will be seeking unspecified consent to use leftover biospecimens for future research, clearly explaining that future research will be in the mental health-related research space to gain a better understanding of the biology unpinning trauma and recovery. Any future studies would need HREC approval before being started and any analysis and distribution of results would be from deidentified and anonymised biospecimens in aggregate (so confidentiality is always maintained). By making this consent optional, participants can make informed choices about their comfort levels with contributing these specific types of data.

5.4 Research Activities

Pre-screen

Individuals interested in participating in the study can complete the pre-screener questionnaire through the UniSC website, which provides preliminary feedback on the likelihood of a PTSD diagnosis. This pre-screening tool is not a formal assessment but can help guide whether an individual should seek a referral. Individuals may also be directly referred to the study by their GP or psychiatrist if there is a strong indication of a PTSD diagnosis or if a diagnosis is already established.

If PTSD is likely, the individual will be scheduled to have a screening phone call with a Mental Health nurse to further assess their suitability. If PTSD is deemed unlikely, alternative community service options will be suggested. Pre-screen questionnaire examples can be found in Appendix E.

Screen

Once potential participants have been identified, the registered mental health nurse or mental health clinician will complete a screener questionnaire over the phone to ascertain whether the individual potentially meets eligibility criteria. Suitability will be assessed against the inclusion and exclusion criteria, and rating scales such as the PCL-5. If successful, the potential participant will be scheduled to come into the TI/NPRC for an in-person clinical assessment with the research team. All potential participants will be advised that a drug and alcohol screen (urine test) will occur on arrival at T1 baseline and again at T5. Potential participants will be advised that they will not be excluded from the study if a positive result is found during the screen but instead the results will be used as a discussion point to understand their substance use and if this may be problematic with propranolol use. The screen materials will be disposed of immediately and only the results collected and stored. Potential participants will be given the RPIS and PICF via email prior to their scheduled appointment. Potential participants should read the RPIS and PICF and discuss it with family members and/or their support network before attending. Screener questionnaires can be found in Appendix E.

Baseline (T1) (Week 0)

The baseline assessment will take approximately 4 hours in total and includes the following:

- Medical assessment (see Appendix D for example questions)
- Psychological assessment:
    - Structured clinical interview (Mini international neuropsychiatric interview)
    - Semi-structured interview

- Pre-assessment self-report questionnaire pack, including demographic questions (see Appendix E for examples questions).

Medical assessment

A medical assessment will be conducted by the study physician onsite to evaluate potential participants' health status. This assessment will screen for any significant medical health concerns (past or present), drug and alcohol use, heart rate variability, comorbid diagnoses, current medication use, and determine if there are any contraindications to the use of propranolol. The assessment will also consider any history of adverse reactions to propranolol, as well as conditions such as asthma, low blood pressure, diabetes, or cardiac concerns. This information will help determine if a potential participant is eligible to safely participate in the study or if they should be referred back to their treating team in the community. For more detailed information, please refer to the physical health assessment in Appendix D.

Pre-treatment self-report questionnaire pack

All potentially eligible participants will be required to complete a series of self-report measures prior to their in-person assessments. Potential participants will be sent a digital link via email for the p*re-treatment self-report questionnaire* pack which will include the following demographic and self-report questionnaires (See Appendix E for full details):

Demographic questions

- Date of birth
- Sex
- Contact details
- Emergency contact information
- Employment status
- Education level
- Current and past medications taken
- Current and past medical history

Self-report questionnaires

- **Peritraumatic distress inventory (PDI)**: 13-item scale measures the level of distress experienced by an individual during and shortly after a traumatic event.
- **Peritraumatic dissociative experiences questionnaire (PDEQ):** 13-item self-reporting scale that assesses an individual's emotional reactions at the time of or immediately after a traumatic event.
- **PTSD Checklist for DSM-5 (PCL-5):** 20-item self-report measure that assesses the 20 DSM-5 symptoms of PTSD.
- **The Impact of Events Scale – Revised (IES-R)**: 22-item measure of the subjective response to a specific traumatic event in an adult or senior population.
- **Beck Depression Inventory (BDI-I):** 21 item self-report scale designed to measure the negative emotional states of depression.
- **Post-traumatic growth inventory (PTGI):** 21-item scale, measuring the level of posttraumatic growth in persons who have survived a traumatic event.
- **Childhood Trauma Questionnaire (CTQ):** 28 item scale measuring an individual's experiences of child abuse and neglect.
- **International Trauma Questionnaires (ITQ):** 18 item self-report measure focusing on the core features of Post Traumatic Stress Disorder (PTSD) and Complex PTSD (CPTSD). It was developed to be consistent with the organising principles of the ICD-11.
- **WHO Quality of life (WHOQOL-Bref):** An abbreviated 26 items assess quality of life (QOL) within the context of an individual's culture, value systems, personal goals, standards and concerns.
- **Pittsburgh Sleep Quality Index (PSQI):** 11 item self-report measure focusing on sleep quality and habits.

Psycho-diagnostic assessment

The psychological evaluation will involve a comprehensive assessment of the potential participant's mental health through a semi-structured interview and further questionnaires. This will include gathering a detailed psychosocial history, which covers aspects such as the participant's social environment, life experiences, and family history of mental health concerns. Additionally, the evaluation will focus on identifying any current mental health conditions, conducting a thorough diagnostic evaluation, and considering any differential diagnoses. This process ensures that a complete understanding of the potential participant's psychological wellbeing is obtained to support accurate diagnosis. The evaluation will also include the following structured clinician-led interview:

- **Mini international neuropsychiatric interview (MINI):** The MINI is a brief structured diagnostic interview for assessing the major psychiatric disorders in the DSM-5 by a lay interviewer.

If potential participants are deemed medically fit and meet full eligibility criteria following the baseline assessment, they will be enrolled in the study and progress to the next phase of the study (T2). Those who do not meet criteria will be referred back to their treating team and provided community support options.
Please note: Once all the data pertaining to eligibility has been finalised (including a diagnosis of PTSD as assessed by the battery of tests in the psychological assessment protocol), and the results of the assessments having been reviewed and approved by the study team, the 'Eligibility Checklist' is completed, and the participant can be enrolled on the waitlist. Participants will then be given an ID Card stating their unique study ID, name of study, study drug, and study site. Participants will be instructed to keep this ID card on their person at all times, so that in the event of emergency (e.g. hospital admission) their treating staff will be aware of their participation in a drug study.

Pre-treatment assessment (T2) and waitlist

After the baseline assessment is completed, participants will be placed on a 4-week waitlist, during which time additional assessments will be completed:

Biological assessment

Biological assessment will be conducted by a study nurse and consist of a basic physical examination and blood sample collection consisting of:

- Height and weight measurement
- General observations; Blood pressure, pulse rate, pulse oximetry, respiratory rate and temperature measurement.
- Blood collection (~30 ml (2 tablespoons) - 2 x 10 ml K2EDTA tubes and 1 x 10 ml SST tube) by a certified phlebotomist in the pathology-certified room located within the National PTSD Research Centre
- Passive drool saliva collection
- Hair clip

Neuropsychological assessment

Cognitive functioning will be assessed using the Cambridge Neuropsychological Test Automated Battery (CANTAB) at pre-treatment (T2), post-treatment (T3) and follow-up 2 (T5). The CANTAB is a fully automated, self-administered neuropsychological test battery presented on an iPad. Once the participant details have been entered, the majority of instructions are delivered by CANTAB and the participant responds as instructed by the CANTAB. Specific cognitive tests were selected due to their known relationship to deficits in PTSD individual's cognition and functioning:

1. Motor Screening Task (MOT) – assess sensorimotor deficits and lack of comprehension,
2. Reaction Time (RTI) – assess reaction time, movement time and motor and mental response speeds,
3. Spatial Working Memory (SWM) – assess retention and manipulation visuospatial information,
4. Paired Associates Learning (PAL) – assess visual memory and new learning, and
5. Rapid Visual Information Processing (RVP) – assess sustained attention.

Magnetic Resonance Imaging (MRI)

Magnetic Resonance Imaging (MRI) is a highly flexible, non-ionising imaging technique that can produce detailed images of the human body, without the use of radiation. As such, there are no radiation exposure or dosage limitations with MRI. This is beneficial, as individuals can be scanned multiple times with no detrimental effect.

All MRI scans will be conducted at the Nola Thompson Centre of Advanced Imaging, located on the ground floor of the Thompson Institute, UniSC. MRI brain scans will be acquired using a 3-Tesla Siemens (Erlangen, Germany) Skyra scanner, with a 64-channel head and neck coil. MRI scans will be acquired by trained radiographers or experienced MR scientists. Our procedures for collecting MRI brain scans will adhere to the Thompson Institutes' "Working with MRI Guideline". Prior to enrolling in the study, all participants will complete an MRI safety questionnaire to ensure participant safety and eligibility (Appendix J). MRI ineligibility is not exclusionary (i.e., participants who do have MRI contraindications can still be enrolled in the study). For each study visit, the MRI safety questionnaire will be completed and reviewed by the trained radiographer or experienced MR scientists. Each MRI scan session is identical, and the duration of each session will be approximately 60 minutes. The MRI scan protocol will include scans designed to measure neuroanatomical structure, dynamic brain activity, and neurochemistry.

Incidental findings from MRI

Prior to consent, participants are informed within the RPIS and PICF (Appendix A and B), that their MRI brain scan is being conducted for research purposes, and as such, is not clinically valid for diagnosis. Importantly, participants are also informed that our research team is not qualified to provide clinical opinions or medical diagnosis based on their brain scans, and reviewing their scans for that purpose is not within our team's scope of practice. However, if a suspected incidental finding or abnormality is identified by our research team or scan operators, we will adhere to the incidental finding policy indicated within the Working with MRI Guideline. Participants are also given the choice to indicate if they would like to be informed of an incidental finding, should one be identified. In short, if a senior research staff involved in the MRI procedure identifies a suspected incidental abnormality, and participants have consented to being notified of this occurrence, this will be communicated to the participant via a phone call from either the principal investigator or a senior member of the clinical research unit. This is the approved policy put forth by the MRI Operations and Safety committee. Participants will be offered a letter addressed to their GP, with a photo of the scan, and may choose to meet with their GP of their own accord. Participants are informed in the PICF, and again in-person, that the MRI scan is not a medical scan, and that research staff are not qualified to make any diagnoses.

Intervention phase (weeks 1 – 6)

Provided that no contraindications to participation were identified in the T1 or T2 assessments, participants will take part in a 6-week treatment period, consisting of once per week RT sessions. If participants miss more than 3 weeks of RT intervention, they will be excluded from the study. Each RT session will last between 25 and 50 minutes per session. Participants will be on their "treatment as usual" regimen which implies that they will continue to take all their regular medications. The propranolol medication used to conduct RT will be adjunctive (as approved by the study GP regarding possible contraindications). Following each treatment session, participants will provide a saliva sample through passive drool collection.

Post-treatment assessment (T3) (week 7 or 8)

The project lead will coordinate with each participant to attend a session at Week 7 or 8 to collect post-treatment assessment measures. See Table 1 for specific assessments completed during this stage.

Follow up 1 (T4) 1 month

The project lead will coordinate with each participant to attend the follow up 1 telehealth session, which will take 50 minutes. This will involve a clinical interview and psychological measures (PCL-5, IES-R, and BDI-I).

Follow up 2 (T5) 3 month

The project lead will coordinate with each participant to attend the 3 month follow up assessment taking approximately 4 hours in total. See Table 1 for specific assessments completed at this stage.

5.5 Discontinuation and Withdrawal

Participants are free to discontinue their participation in the study at any time, without prejudice to further treatment. Participants who discontinue from the study will always be asked about the reason(s) for their discontinuation and about the presence of any adverse events. If possible, they will be seen and assessed by an

Investigator and complete the withdrawal of informed consent procedure (see Appendix B; PICF). Where participants are not willing to continue any research assessments, they will be considered withdrawn from the study. Adverse events will be followed up until resolution, the adverse event stabilises, or the participant is lost to follow up.

Participant discontinuation criteria

Participants will be discontinued from participating in the study in the following circumstances and, if in need, be referred to their primary medical officer

1. Participants who develop any complications during the study
2. Participants who become too vulnerable or fragile during the study
3. Participants who miss more than 3 weeks of the treatment sessions
4. Participants who do not have a treating team

Discontinuation of parts of this study or the entire study will be considered if new information about reconsolidation therapy becomes known to the researchers.

Escalation procedure

If a participant develops a known (or previously undocumented) adverse reaction to the treatment during the study, clinical and research staff will refer to the *Recognising and Responding to Physiological deterioration SOP* which will include some or all of the following:

- Appropriate and timely medical care is provided by trained and qualified staff. If required, the emergency services (Queensland Ambulance Services – QSA) and UniSC security are contacted immediately.
- Attending registered nurse will monitor physiological signs and symptoms on initial session.
- If the ambulance service is not required, the participant will be referred for consultation with their GP and their participation from the study will be withdrawn.
- If the ambulance service is required for immediate medical admission, the clinical and research staff will supply relevant patient information to assist with participant treatment and monitoring.
- Escalation, either hospital admission or GP referral, will be coordinated by the Registered Nurse with support from technical and research staff of the Thompson Institute. Any escalation will require an immediate (within 1-day) staff meeting, to debrief, check on staff welfare, review processes and procedures, and ensure all appropriate adverse event documentation is completed in line with stipulations in section 10 (safety measures).

If a participant's mental health condition significantly deteriorates during the study, the clinical and research staff will refer to the *Recognising and Responding to Deterioration of Mental state – Operating Procedure, and Escalation of Care Guidelines* which will include some of all of the following*:*

- Assessment of mental health condition (Mental State Examination by qualified clinician)
- Clinician assessment of indicators and signs of deterioration including:
    - any reported changes,
    - signs of distress,
    - loss of touch with reality or consequence of behaviours,
    - loss of function,
    - dissociation
    - elevated risk to self, others or property.
- Call 000 for emergency response
- De-escalation and management of increased physical aggression
- Contact made with participants GP and other members of treating team
- Referral to acute mental health services as required

Withdrawal criteria

Participants may withdraw at any time during the study. A participant will be considered 'withdrawn' from the study in cases where all involvement is ceased. A participant will be withdrawn in the following cases:

1. Revocation of consent
2. The site PI believes that it is in the best interest of the participant to be withdrawn.

Should either of the above situations take place, withdrawal will occur immediately.

5.6 Safety Measures

The TI/NPRC has Standard Operating Procedures (SOP) in place to manage adverse and severe adverse events, complaints and feedback and medical emergencies. The PI is required to ensure all study staff are aware of the definitions and procedures in the SOP. Summary details of the SOP can be found in Appendix I.

5.7 Study Risks

Several risks, inconveniences and potentials for distress have been identified as a part of this study. As such, the researchers have employed methods to mitigate these risks, which are outlined below. Prior to study commencement, a risk assessment meeting will be conducted with key study personnel (CIs, AIs and study-specific new hires) to comprehensively identify risks and management and mitigation strategies. Identified risks associated with this study will be added to the site-specific project risk registers. The TI/NPRC will utilise UniSC's established risk framework inclusive of a risk matrix (Likelihood: Almost Certain – Rare; Consequences: Catastrophic – Insignificant) to calculate both inherent and residual risks. Further guiding policies that aid in determining risk likelihood and consequence, as well as UniSC's Risk and Compliance Manual, will be fundamental resources for this project.

Potential harms: Propranolol use

There is risk of minor physical side effects associated with propranolol medication as outlined in the RPIS and PICF (see Appendix A and B)**.** Potential side effects include lowered blood pressure, nausea, dizziness, and fatigue.

Potential harms: Economic

The participants may incur costs in accessing transport to and from the Thompson Institute. If employed, participants may forgo hours worked at employment to attend treatments.

Potential harms: Diagnostic, psychological, cognitive measures

Recruitment of participants who might have undiagnosed disorder which is marked as exclusion criteria (e.g., asthma, diabetes, severe psychiatric condition).

Participants will be asked to complete several questionnaires assessing their behaviours, cognitive function, and emotions and feelings. Whilst there are no anticipated risks associated with participation in this research, we do acknowledge the possible anxiety or other psychological distress which may arise when these topics are discussed.

Potential harms: Discomfort and inconvenience

Participants may feel anxious or distressed about the treatment because of it not being commonly used practice in clinical setting. Participants may experience stress, distress, discomfort and/or anxiety in undertaking the neuropsychological assessment and in answering various questions. Participants may experience anxiety and/or claustrophobia when undertaking the MRI. Participants may be inconvenienced by giving up the time required to participate in the research and to recuperate after the treatment session. Participants may be uncomfortable with needles and/or having blood drawn or may experience minor pain at the time of needle insertion.

Minimising risk: Propranolol use

All relevant research team members will have the skills needed for responding to a hypotensive event and Cardiopulmonary resuscitation. Research assistants and other staff members will be required to have a current CPR certification. We will ensure that participants are provided with an accurate and fair description of the risks or discomforts and the anticipated benefits. These are outlined in the RPIS and PICF (see Appendix A and B). The Thompson Institute is appropriately equipped to accommodate participants who are nauseous, vomiting or dizzy.

During referral, acceptance, treatment, and follow-up phases we will assess participants to determine if they pose imminent risk to themselves or others. If so, participants will be referred for immediate intervention and withdrawn from the study.

Minimising risk: Psychological

To mitigate any negative effects of the study measures, care will be taken when administering questionnaires and measures. If any stress or discomfort is observed the participant will be given the option of taking a break and returning to the test/questionnaire later. Where significant distress occurs, we may enlist the assistance of an on-site clinician to assist with reducing discomfort/stress as needed.

If psychological effects are experienced, relevant staff are trained to minimise distress quickly and effectively to participants. This can include de-escalation, psychoeducation, reassurance, implementing a relaxation procedure, grounding methods, and other treatments.

If a potential participant is identified as too vulnerable or fragile to partake in the study, they will not be allowed to be part of it. If a participant becomes vulnerable or fragile during the study, they will be discontinued. This decision will be conveyed to them by a senior staff member in a professional and caring manner.

If any participant indicates they are experiencing a high level of stress or emotional distress, or if they exhibit behaviours suggesting that they are going through a stressful time, we will confirm if this is related to the research or other life events. Irrespective of the cause the mental health clinicians will provide support or referral to assist them to gain stability. To accomplish this, we may need to (with the participant's consent) contact a family member, a referring source, or a member of the health care team treating them for further advice/ support. We may need to provide information regarding independent psychological or social services or refer the participant to an independent mental health practitioner.

We will regularly monitor the participants to be aware of any potential for emotional exhaustion, feeling overwhelmed, or worsening of their mental state during the study as they may be under risk of re-experiencing or revealing potential past psychological traumas, or at risk of exacerbating their psychological symptoms. A suitably qualified member of the research team may engage the participants in therapeutic strategies to reduce discomfort/stress as needed.

Minimising risk: Discomfort and inconvenience

The neuropsychological assessments will be scored by a qualified clinician. Self-rated scales may be completed in the presence of research staff. These scales are an integral part of the research, and the perceived benefits outweigh the risks. Before the questions on the scales are asked, we will advise participants that they are welcome to initiate a break at any time if they are anxious or feel discomfort answering the questions.

In instances of claustrophobia or where the participant has indicated distress/discomfort during the MRI, an eye mask will be available, and the participant will be closely monitored. Our senior MRI radiographers have extensive experience in dealing with anxious participants.

Minimising risk: Economic

We will attempt to ensure that the research does not cause social or financial risks or loss to participants. If participants are disadvantaged financially in terms of cost of transportation during research participation, petrol vouchers can be provided. Any payments made to participants (for participating in the assessments) will not adversely influence the design, conduct, findings or publication of the research.

Mandatory reporting

All staff at TI are required to complete mandatory training every two years (at a minimum) in relation to child safety. The ***Child Protection Act 1999*** requires certain professionals (mandatory reporters), to make a report to Child Safety, if they have a reasonable suspicion that a child has suffered, is suffering or is at an unacceptable risk of suffering significant harm caused by physical or sexual abuse, and may not have a parent able and/or willing to protect them. The following plan will be implemented to manage information that triggers mandatory reporting requirements.

1. All medical officers and registered nurses undergo annual mandatory training on Queensland's mandatory reporting requirements as outlined by the Department of Children, Youth Justice and Multicultural Affairs. This training covers recognising reportable incidents, understanding the legal obligations, and the process for reporting.

2. A clear reporting pathway will ensure a prompt notification to the appropriate authorities. A medical officer or registered nurse will, as soon as possible inform Trish Wilson (co-investigator and designated safeguarding officer) upon identifying information that may necessitate mandatory reporting. It will be determined if this information constitutes a 'reasonable suspicion' and if so, a report will be made to Child Safety on 1300 703 762.
3. Any information flagged for mandatory reporting will be documented appropriately, maintaining confidentiality and sensitivity toward the participant's privacy. Only the necessary information required for reporting will be shared with authorities.
4. Team members exposed to potentially distressing information will have access to support resources to manage the emotional impact.

5.8 Potential Study Benefits

Potential benefits to participants taking part in the study include:

- The treatment will impose positive effects on the participant and reduce PTSD symptoms
- The feedback and data collected will assist in evaluating the clinical utility of the treatment.

5.9 Data Collection/Gathering

The study will be collecting mental health information, biospecimens and neurological information of its participants. Collection will take place on site at the UniSC Thompson Institute campus by trained research personnel. The RPIS, consent form, and questionnaire measures will be created in and delivered via Qualtrics, using the research team's password protected UniSC Qualtrics account. Qualtrics is a UniSC approved site and stored survey answers can only be accessed using the researcher's password-protected USC-Qualtrics account.

5.10 Data Management and analysis

Once completed, screening for the total number of completed surveys will take place and we will ensure no personal details (names, contact details etc) are associated with the survey information. All data collected will be stored in line with the UniSC Research Data Management Procedures.

A unique code will be generated for each participant enrolled in the study to de-identify data. The information for linking unique codes to participant contact information will be made accessible to necessary project staff for the purposes of scheduling assessments. All electronic data will be stored securely on computers at the TI/NPRC or on secure research specific databases. Only researchers will have access to the data and other research documents. The computers will be secured by usernames and passwords and protected from external access. Hard copy documents, material, and data will be kept in a locked filing cabinet, inside a locked office. All paper records will be securely converted to pdf files to mitigate the risk of data loss through an emergency (e.g. fire or flood).

Re-identifiable data (using the unique code identifiers) will be exported from Qualtrics to IBM SPSS for analysis. Statistical analyses will include generalised linear models (GLMs), analysis of the relative change index and frequentist statistics. A significance level of $p < .05$ (two-sided test) will be utilised where required. Data will be inspected for outliers and any spurious data will be corrected or removed prior to analysis. A detailed data analysis plan will be constructed by a statistician including the research questions and variables included. Missing data will be examined for missingness patterns. If the data is missing at random or completely at random, data imputation strategies may be employed in order to protect the integrity of this longitudinal sample and statistical power. Data will be analysed using descriptive, bivariate, and multivariate statistics using intent-to-treat analyses.

All material will be kept for at least 15 years from the publication of results, as per national requirements, and then disposed of using secure destruction methods such as shredding of paper data and erasure of computer-generated data. Our main priority will be the protection of participants' confidentiality and the compliance with their informed consents. No participants will be identifiable in abstracts, oral presentations, posters, manuscripts, trial reports, or documents. If a participant requests that their data is withdrawn, the research team will ensure their data is appropriately located and removed.

Biospecimens will be stored in the Thompson Institute/National PTSD Research Centre molecular biology laboratory. Access to the lab is strictly restricted and controlled by UniSC security. Samples will be tested for genetic and expressed/circulating markers using established molecular biology techniques and under the approval of UniSC risk assessments. Any unused sample from a test will be disposed of through approved UniSC biohazard waste disposal protocols (incineration via an established service provider). Biospecimens are labelled with deidentified IDs and processed anonymously in the laboratory setting, with no identifiable information associated with the biospecimens during routine handling or disposal to respect personal and cultural sensitivities. The master document containing identifiable information will be stored in secure UniSC servers and be password protected. The RPIS contains a comment section that allows for any personal or cultural sensitivities relating to biospecimen handling to be captured and implemented by the research team.

Biospecimens are labelled with deidentified IDs and processed anonymously in the laboratory setting, with no identifiable information associated with the biospecimens during routine handling or disposal. The master document containing identifiable information will be stored in secure UniSC servers and be password protected. Only authorised study staff will have access to the identifiable master document. The research being conducted with these biospecimens has no diagnostic value and results will not impact participants health decisions or those of there relatives or community.

Any research collaboration regarding these biospecimens or the data generated from them will require a formal collaborative agreement with UniSC and UniSC ethics and guidelines will govern biospecimen management.

Participants are free to withdraw consent at any time, for any reason. Any biospecimen material remaining at the time of withdrawal will be destroyed as per waste disposal guidelines. Any data generated prior to the withdrawal of consent that is identifiable will be destroyed/deleted. However, data that has been deidentified and aggregated for analysis prior to withdrawal of consent cannot be reidentified and removed at this point, so that data will remain within the analysis in an unidentifiable manner. There are no financial or personal interests to be gained by participants in this study regarding their biospecimens. There are no commercial applications expected from this research.

5.11 Clinical Trials

Propranolol (Inderal®) is manufactured by Wagner Pharmaceuticals Inc. and Apotex Pty Ltd and is supplied as a prescription-only medicine available through pharmacies. INDERAL tablets are available in 10 mg and 40 mg doses of propranolol hydrochloride, intended for oral administration. Propranolol is listed on the Australian Register of Therapeutic Goods (ARTG) as a therapeutic substance. We will be seeking approval from the TGA for use of propranolol 'off label' in the clinical trial under the supervision of the study physician (GP).

Approved therapeutic indications

Approved therapeutic indications include:

- Angina pectoris
- Hypertension
- Prevention of migraine
- Cardiac dysrhythmias: for treating specific intrinsic cardiac dysrhythmias, dysrhythmias associated with thyrotoxicosis, anxiety-induced tachycardia, and certain drug-induced dysrhythmias, such as tachycardia caused by digitalis or adrenaline overdosage.
- Essential tremor, including familial and senile tremor
- Phaeochromocytoma (to be used only with concurrent α-receptor blockade)
- Hypertrophic subaortic stenosis
- Suspected or definite myocardial infarction
- Fallot's tetralogy

Mechanism of action

Propranolol hydrochloride is a β-adrenoreceptor blocking agent that acts non-selectively on both β1 and β2 receptors. It has minimal intrinsic sympathomimetic activity and exhibits some membrane-stabilizing properties. INDERAL is a racemic mixture, with the S(-) isomer being the active form of propranolol. The primary effect of propranolol hydrochloride is to diminish the impact of excessive sympathetic nervous stimulation on the heart, leading to a reduction in pulse rate, cardiac contraction force, and cardiac output. This, in turn, significantly decreases myocardial oxygen demand, to a greater extent than the reduction in workload. These combined effects offer therapeutic value in the treatment of several cardiovascular conditions.

The mechanism by which propranolol hydrochloride lowers elevated blood pressure remains unknown. However, the drug has been shown to inhibit exercise-induced tachycardia, with this effect being directly related to its plasma concentration. Notably, no correlation has been established between the plasma concentration of propranolol and its antihypertensive effects.

The anti-anginal activity of propranolol hydrochloride likely stems from a reduction in left ventricular work and oxygen utilization due to the inhibition of cardiac sympathetic nerve stimulation. Propranolol hydrochloride has also demonstrated serotonin antagonism, though the therapeutic benefit of this property in centrally mediated disorders is still uncertain. As with other β-adrenoreceptor blocking agents, propranolol hydrochloride has negative inotropic effects, and therefore, it is contraindicated in patients with congestive heart failure.

Known adverse events

Propranolol hydrochloride is usually well tolerated, and side effects are transient in nature, rarely necessitating withdrawal of treatment. The most serious adverse reactions encountered are congestive heart failure and bronchospasm in susceptible patients. Common adverse reactions include fatigue and/or lassitude (often transient), bradycardia, cold extremities and exacerbation of Raynaud's phenomenon, sleep disturbances including vivid dreams/nightmares. Other less frequently reported adverse reactions include gastrointestinal disturbances (nausea, vomiting, diarrhoea, abdominal pain), congestive heart failure, dizziness, bronchospasm. Rare cases of thrombocytopenia and purpura have been reported. CNS symptoms including mood changes and hallucinations have been reported rarely. If should be noted that those symptoms have been reported among individuals taking propranolol every day for prolonged periods of time. Our study participants will be taking propranolol once a week, for 6 weeks.

Known contraindications or warnings:

- **Cardiovascular**:
    - Congestive heart failure
    - Right ventricular failure secondary to pulmonary hypertension
    - Significant right ventricular hypertrophy
    - Sick sinus syndrome
    - Sinus bradycardia (less than 45 to 50 beats/minute)
    - Second- and third-degree A-V block
    - Hypotension
    - Severe peripheral arterial circulatory disturbances
    - Prinzmetal's angina
- **Hypoglycaemia, prolonged fasting and metabolic acidosis:**
    - Propranolol must not be used in patients prone to hypoglycaemia, i.e. patients after prolonged fasting or patients with restricted counter regulatory reserves. In metabolic acidosis (e.g., in diabetes), the premonitory signs of hypoglycaemia may be masked in patients receiving hypoglycaemic agents.
- **Asthma/bronchospasm:**
    - β-adrenergic blockade of the smooth muscle of bronchi and bronchioles may result in an increased airways resistance. These drugs also reduce the effectiveness of asthma treatment. This may be dangerous in susceptible patients. Therefore β-blockers are contraindicated in any patient with a history of bronchial asthma, airways obstruction or a tendency to bronchospasm. Use of

cardioselective β-blockers can also result in severe bronchospasm. If such therapy must be used, great caution should be exercised. Alternative therapy should be considered.

- **Other:**
    - Allergic disorders (including allergic rhinitis) which may suggest a predisposition to asthma or bronchospasm
    - Shock (including cardiogenic and hypovolaemic shock)
    - Hypersensitivity to the drug
    - Anaesthesia with agents that produce myocardial depression (e.g., ether, chloroform)
    - Untreated phaeochromocytoma

Pharmacokinetics

- **Absorption:** Studies with propranolol hydrochloride in humans indicate that it is almost completely absorbed from the intestine. A large part of the absorbed drug is lost to systemic circulation due to the first pass metabolism in the liver. After repeated administration, the first pass removal process becomes saturated and, at steady state, the plasma concentration is proportional to the dose, although there is some variation between patients as to the blood levels achieved at a given dose. In addition, correlation of plasma level to therapeutic effect varies considerably with propranolol as with some other β-blockers. Blood level measurements show that after intravenous administration, the concentration in the circulation decreases rapidly due mainly to uptake by tissues generally.
- **Bioavailability:** In general, the peak blood level occurs between 1 and 3 hours after oral administration and will have an average value of 0.1 µg/mL per 80 mg single dose. The peak blood level is proportional to the dose. With chronic administration the mean plasma half-life is from 3 to 6 hours, determined by clearance and plasma binding. Following intravenous administration, the plasma half-life of propranolol is about 2 hours and the ratio of metabolites to parent drug in the blood is lower than after oral administration. In particular 4-hydroxypropranolol is not present after intravenous administration.
- **Distribution:** Propranolol is absorbed from the circulation and is widely distributed throughout the body tissues.
- **Protein binding**: Approximately 93% is plasma bound in humans.
- **Metabolism:** Propranolol is completely metabolised, primarily by the liver. Hydroxylation of the aromatic nucleus occurs with degradation of the isoprenaline side chain. Over 20 metabolites have been identified. One of these, the 4-hydroxy metabolite, found only after oral administration has β-adrenergic blocking properties.
- **Excretion:** Some 95 to 100% of a dose of propranolol hydrochloride is excreted as metabolites and their conjugates in the urine.
- **Half-life:** The plasma half-life of oral propranolol is of the order of 3 to 6 hours. The pharmacological effect lasts much longer.

Please see Appendix G for interactions with other medicines and special warnings.

6. Results, Outcomes and Future Plans

At the time of submission, the project timeline estimates that participant data collection will be completed by the end of 2027. At the close of data collection, all data will be entered and saved on secure TI/NPRC servers, accessible only to the PI and authorised research members. All research staff involved in data collection and/or management who subsequently leave the research study will have access to all electronic data revoked.

Disseminating general study findings to the participants and their families is of a high priority. Our participants will be given the option to receive general results from the study by requesting these from their referring medical officer. This will assist the patients in the future if they want to use this treatment option as part of their management; it also allows their participation, commitment, and contribution to literature and science to be acknowledged and valued. Individual results will not be available to participants and UniSC retains ownership of all data produced as a result of this research.

Data generated from this research will be published in relevant academic journal articles, both as part of PhD student's thesis and research output of post-doctoral researchers at the Thompson Institute. The findings of this report will be readily accessible to staff and students at the TI/NPRC.

All publications and presentations will only report aggregate de-identified data, with no identifiable information published at any point. We expect this study will receive widespread public interest and media attention, enabling public dissemination of findings. There are no anticipated restrictions on publication of results from this research. We are open to share the information and key implications with the community, relevant authorities, local clinical organisations, and other stakeholders to realise the potential benefit of results with the wider community, and on international grounds, especially for sufferers, their families, and carers. In that respect, we will also ensure participant confidentiality and protect the intellectual property rights of the TI/NPRC.

To the extent allowed by the conditions of ethical approval, participant consent, funding, and legislative stipulations, we are open to sharing information relating to study design, resources and results with research entities and/or psychiatric/psychological practices which request access. If information is shared, all data and results will remain de-identified and only the data of those participants who consented to the sharing of their data will be included. Participants are informed of all planned sharing and future data use in the PICF. By signing this form, they are indicating this has been explained to them and that they understand.

7. Appendix

7.1 Appendix A: Research Participant Information Sheet (RPIS)

Research Project Information Sheet

Examining the biopsychosocial predictors of treatment response to propranolol-based reconsolidation therapy for trauma- and stressor-related (TSR) disorders.

Ethics Approval Number: **XXXXXXX**

Research Team Contact Details

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Project Description

The purpose of this research project is to study the therapeutic effects of memory reconsolidation blockade (propranolol combined with script-driven trauma recall) on the reduction of post-traumatic stress disorder (PTSD) symptoms and diagnosis. You have been referred to us as a possible participant for this study because you have been experiencing mental ill-health due to previous experience/s of trauma. This study will test reconsolidation blockade treatment (RT) as an adjunct treatment for people experiencing PTSD and associated symptoms.

If you meet the following inclusion criteria below, you are invited to participate in this research study.

- 18years or older
- Have a diagnosis of PTSD
- Can understand this information sheet and provide written informed consent
- Able to undertake psychological, cognitive, and biological assessments
- Able to tolerate oral propranolol and not be taking any drugs that could contraindicate propranolol
- Have a current treating team who is managing your mental health
- If you have child-bearing potential, you must agree to use a highly effective method of contraception (e.g., oral contraceptives containing combined estrogen and progesterone, bilateral tubal occlusion, vasectomy). **Note**: Highly effective contraceptive use is an inclusion criterion for this clinical trial to ensure participant safety and prevent potential risks to fetal development, as propranolol may pose risks if inadvertently administered during pregnancy

Please note, you will be unable to participate in the study if you meet any of the following exclusion criteria below:

- Have a diagnosis of Complex PTSD
- Have a significant psychiatric disorder (e.g., Bipolar Disorder, Personality Disorder, Psychosis, Substance Use Disorder)
- Any contraindication to propranolol as determined by the study physician
- Development of serious, adverse, or unexpected events/reactions during the trial
- Previous allergy or reaction to propranolol, or other beta-adrenergic blocking agent
- Participation in any other clinical study at the time of enrolment, or having received any investigation product within 30 days of the day of enrolment onto the study
- Currently pregnant, breastfeeding or intending to become pregnant during the course of the study.

Any other condition that, in the opinion of the investigator, may adversely impact the safety of the participant or the accuracy of the study data

Participation
As a participant in this study, you may benefit from the treatment in terms of improvement in reduced PTSD symptoms. However, there is no guarantee or promise that you will experience any improvement and there is the potential for you to experience some minor side effects which are detailed below. Participating in this study requires a significant time commitment. If you are identified as too vulnerable or fragile to partake in the study, you will not be allowed to be part of the study. If you become vulnerable or fragile during the study, you will be discontinued from the study. We therefore strongly encourage you to involve your treating doctor, family members, carers, and/or a support person when deciding whether you would like to participate or not. Note, a support person may be present with you during the research study to provide assistance and comfort as needed.

If you indicate that you are experiencing a high level of stress or emotional distress, or if you exhibit behaviours suggesting that you are going through a stressful time, we may need to (with your consent) contact a family member, a referring source, or a member of your health care team for further advice/ support. We may need to provide information regarding independent psychological or social services or refer you to the Acute Mental Health Care team.

Why is the study being conducted?
The purpose of the current study is to determine:

- The effectiveness of reconsolidation blockade treatment (i.e. recalling trauma under propranolol) in reducing PTSD symptomatology in adult participants
- The psychosocial, cognitive, and neurobiological effects of oral propranolol and script driven trauma recall in adult participants with PTSD

What is propranolol and how is it presently used?
Propranolol belongs to a group of medicines known as a beta-blocker, which is primarily used to treat a range of cardiovascular conditions such as high blood pressure (hypertension), angina (chest pain), and irregular heartbeats. It works by blocking beta receptors in the heart and other parts of the body, including the brain, which reduces the effects of adrenaline and other stress hormones, leading to a slower heart rate and reduced blood pressure. Propranolol is not a psychotropic drug

In addition to its cardiovascular uses, propranolol is sometimes prescribed off-label for conditions like anxiety, migraine prevention, and tremors. It can help reduce the physical symptoms of anxiety, such as rapid heartbeat and shaking, making it particularly useful in performance or situational anxiety contexts.

What is involved in participating in a clinical trial?
If you agree to participate in this research project, you will be asked to do all of the following:

- a screener telephone interview,
- a baseline assessment,
- a pre-treatment assessment (after a 4-week waitlist),
- 6 consecutive weeks of treatment, involving off-label use of propranolol facilitated by the study doctor.
- a post-treatment assessment, and
- 2 x follow up assessments (1 month by phone and 3 months in person)

Table 1. What is involved in the study. N**ote**: Your participation is voluntary, and you may withdraw at any stage. The Thompson Institute also reserves the right to discontinue your participation in the study at any time for any reason it determines that is in your or study staff and other participants, best interests.

What will you do	**Screen**	**T1 Baseline Week 0**	**T2 Pre-treatment 4-week waitlist**	**Intervention Weeks 1–6**	**T3 Post-treatment Week 7 or 8**	**T4 Follow up 1 1-month**	**T5 Follow up 2 3-month**
Time required	30-min phone call	4-hour clinical assessment	4-hour clinical assessment	Once weekly 25-minute RT session over 6 weeks.	4-hour clinical assessment	50-min clinical interview	4-hour clinical assessment
Setting	Tele-health	UniSC	UniSC	UniSC	UniSC	Telehealth	UniSC
Activity	Interview	Medical tests Psychological tests	MRI* Biological tests	Propranolol dosage 60mins	MRI Biological tests	Psychological tests	MRI Biological tests

			Neuropsychological tests Psychological tests Hair clip	before session Script-driven recall in session Saliva	Neuropsychological tests Psychological tests		Neuropsychological tests Psychological tests Hair clip
Consent	Written consent form provided at T1						
Withdraw	At any point up until the data has been analysed and aggregated.						

*MRI – Magnetic resonance imaging.

Reconsolidation blockade treatment:
As a participant in this study, you will receive a 6-week course of oral propranolol in addition to the prescribed psychotropic medication you are already receiving, if any. Propranolol treatment involves an oral propranolol dose given once per week, 60 minutes before your scheduled treatment session. The dose you receive will depend on your weight and the dose will be titrated (adjusted to find the ideal balance).

NOTE: You cannot have propranolol treatment:
- If you have ever had a negative reaction to propranolol
- If you have diabetes, asthma, heart disease, or low blood pressure
- If the study doctor determines that it is not safe, or not in your best interest to receive propranolol

Propranolol: Possible risks, side effects and discomforts
As with any medication, propranolol can produce side effects, although not everyone experiences them. The main side effects of propranolol include (but are not limited to):
- Temporary decrease in blood pressure and pulse rate.
- Tiredness or fatigue
- Dizziness
- Cold hands and feet
- Some people may experience nausea, stomach cramps, or diarrhea.
- Bronchoconstriction (spasm of the airways making it difficult to breathe)

There is a small risk of experiencing a severe allergic reaction (anaphylaxis) when taking propranolol. Symptoms of an allergic reaction may include rash, itching, swelling (especially of the face, tongue, or throat), severe dizziness, and difficulty breathing. While severe allergic reactions to propranolol are rare, they can be life-threatening and require immediate medical attention. If you experience any signs of an allergic reaction, which involve difficulty breathing, if you are in our care advise us immediately and we will apply emergency medical care right away. Otherwise if you are at home or elsewhere, please seek immediate emergency medical care. If you experience any of the other symptoms above please advise the research team immediately and make them aware if have a history of allergies, particularly to medications, and also see, follow up medical care.

What about other medications?
In this study, you will not be asked to discontinue your usual medications prescribed by your primary health practitioners. It is also crucial for you to attend any and all follow up appointments with your primary health practitioner and continue administering your usual medications.

Medical tests
At the baseline assessment (T1), you will have a thorough health check conducted by the study physician (GP) to make sure it is safe for you to participate in the study. This assessment will look at your overall health, including any past or current medical conditions, other diagnoses you may have, and your current medications. The doctor will check for any conditions that might make taking propranolol unsafe for you, such as asthma, low blood pressure, diabetes, or heart issues. They will also ask if you've had any negative reactions to propranolol before. The doctor will also complete a drug and alcohol screen (urine test) at T1 and T5. If a positive result is found, you will not be excluded

from the study. We will use this information to understand your substance use and how this may affect propranolol use during the study. This information will help us decide if you can safely take part in the study or if you would be better supported by being referred back to your primary health practitioner and regular healthcare team.

Psychological tests
Throughout this study, we will require you to undertake several self-report and clinician-administered questionnaires. Some of these questionnaires are designed to collect demographic and safety monitoring data, whereas others will assess psychological symptoms, the severity and impact of those symptoms, and overall quality of life. **Please note**: You may experience some discomfort and anxiety in undertaking the psychological assessment and in answering questions during the various scales.

Biological tests
Blood
As part of this study, we will require drawing blood from you. These are taken at different time points throughout the study. The blood tests are an important part of our research data and will help us answer molecular biology questions related to trauma exposure and symptoms. To be a participant in this study, you must be comfortable to provide these blood tests. The blood collection will take place on-site at the Thompson Institute. Staff from the research study will collect the blood as per the Thompson Institute standard procedure. All blood collected, will be analysed and disposed of by the Thompson Institute. The phelebotomist will draw approximately 45 millilitres of blood (three tablespoons) at the baseline and follow up visits for clinical and safety purposes. In total, blood will be collected at T2, T3, and T5 visit timepoints.

Once collected, the blood samples will be transported by Thompson Institute staff to the University of the Sunshine Coast lab for temperature-controlled storage until future testing can be completed. The blood samples will be labelled in re-identifiable form using your research ID code, but not with your name. With your consent, the data and bloods from this study may be available for further UniSC studies. These studies may include biological and genetic analysis to understand why some people respond to treatment and why some people do not. There may be a small risk the genetic material reveals some adverse health information unrelated to these studies. This information will be kept confidential and de-identified, published findings relating to this research will not reveal the identity of any participant. None of the blood analyses being conducted have clinical implications at this time and are being examined for research purposes only. **Please note**: You may experience minor discomfort associated with having blood taken and you should not use the arm from which blood was taken for 12 hours after collection.

Saliva
As part of this research, we will require saliva collection from you. The samples will be required at T2, after each treatment session, T3, and T5 visits. To be a participant in this study, you must be comfortable to provide these samples. The samples you provide will be handled by the study nurse and the molecular biology scientists. Collection will use the passive drool technique.

Hair Clip
As part of this study, we will collect a small strand of hair from you at the first and final time points (T2 and T5) to measure cortisol levels. Cortisol is a hormone related to stress and analysing it from hair samples provides valuable insights into long-term stress patterns. The hair sample will be taken using a non-invasive method, requiring a few strands cut close to the scalp, and you can decline to provide a sample at any time without affecting your involvement in the study.

Please note: we will be seeking your consent to use any leftover biospecimens collected in this study for use in future mental health-related research to gain a better understanding of the biology underpinning trauma and recovery.

Neuroimaging tests
Magnetic Resonance Imaging (MRI)
This is a non-invasive procedure that involves laying in an MRI scanner while images of brain structure and activity are recorded. The MRI scan will take about one hour and be done at visits T2, T3 and T5. A scan operator will guide you through the MRI scan. You will be asked to change into MRI safe scrubs and to remove any jewellery or objects containing metal. Your personal items will be stored in a locked cupboard during the MRI.

Sometimes people can experience distress or claustrophobia during an MRI. Our research team will show you all of the facilities including the MRI control room (with a view of the scanner) before your scan session. In instances of claustrophobia or where you feel distress, anxiety or discomfort, our research team will assist you, provide reassurance and answer any questions. An eye mask can be provided to you, or an option to watch a nature documentary or listen to music can also be provided. These options have been found to help participants who are feeling anxious. At all times you will be closely monitored and there is two-way communication with the scan operator and research team during the MRI scan. If you feel uncomfortable undertaking the MRI scan, the scan will be discontinued, and this will not affect your participation in the overall study.

Please find here a short video reviewing what to expect at your first scan: https://www.usc.edu.au/thompson-institute/research-at-the-thompson-institute/nola-thompson-centre-for-advanced-imaging

It is important to note that this research scan is not diagnostic. Therefore, we will not be actively looking for any abnormalities or pathology. If a researcher does coincidentally identify a potential anomaly that may require further investigation, we endeavour to contact you so that you may seek independent medical advice. However, it is important that you understand that you should not rely on the researcher to review the scan for diagnostic purposes, and the Thompson Institute is not responsible for ensuring you or your regular doctor is notified of unrelated adverse scan findings and that you should seek independent medical advice in the event you have any health concerns. The MRI will be completed three times during the study at T2, T3 and T5visits.

Neuropsychological tests
As part of this study, your cognitive abilities will be assessed). To do this, we will be using the Cambridge Neuropsychological Test Automated Battery (CANTAB), which includes several tasks specifically selected to measure different areas of brain function that may be affected in people with PTSD. The tasks are activities with instructions that you complete on an iPad and include:

- **Motor Screening Task (MOT)**: Measures basic movement and coordination skills, as well as your understanding of the instructions.
- **Reaction Time (RTI)**: Assesses how quickly and accurately you can respond to visual prompts.
- **Spatial Working Memory (SWM)**: Tests your ability to remember and use visual information in short-term memory.
- **Paired Associates Learning (PAL)**: Measures your ability to learn and recall visual information.
- **Rapid Visual Information Processing (RVP)**: Evaluates your ability to maintain attention and focus over a period of time.

These assessments will be completed on-site and you will have a member of the research team in the room to assist you if you have any questions. The CANTAB will help us better understand how PTSD may impact thinking and learning processes and will be completed three times during the study at T2, T3 and T5 visits.

Will I incur any cost participating in the study?
There will be no cost to you for participating in the study.

Possible benefits from participating in the study
Overall, the treatment provided in this study may reduce the intensity and frequency of PTSD symptoms. Possible secondary outcomes include improvement of functioning and wellbeing. The findings from this research may prove that this is an effective treatment for PTSD, and this may benefit the wider community of PTSD sufferers in the future and help to save lives.

New information arising during the study
During this study, new information about the risks and benefits of propranolol may become known to the researchers. If this occurs, you will be told about this new information. New information may mean that you can no longer participate in this study. If this occurs, we will discontinue your study participation. In all cases, you will be offered all available care to suit your needs and medical condition.

Maintaining your own treating team
Participation in this study does not replace any current treatment or therapeutic support you are receiving, and it is your responsibility to maintain contact with your existing treating healthcare team including regular GP, throughout

the duration of the study. If it is found that you do not have a treating team at any point during the study, your participation in the study will be discontinued.

Information ownership
You will not own the results, research data, or the sample you provide to the researchers throughout the study. All tests and scans performed in this study are for research purposes and not for diagnostic purposes. As such, the researchers will not be able to discuss your individual study findings with you.

Permission to video record sessions
We will ask for your permission to video record your treatment sessions. These recordings will be used for educational and teaching purposes to help improve the training of students and healthcare professionals. They will be shown at conferences for further education and teaching purposes and will enhance our understanding of effective treatment approaches. Your privacy and confidentiality are our top priorities, and any identifying information will be removed before use. Participation in the recordings is completely voluntary, and you can choose to decline or withdraw your consent at any time without it affecting your care in the study.

Participation discontinuation criteria
Participants will be discontinued from participating in the study in the following circumstances and, if in need, be referred to their primary medical officer

- Participants who develop any complications during the study
- Participants who become too vulnerable or fragile during the study
- Participants who miss more than 3 weeks of the treatment sessions

Participants who do not have a treating team involved with their care.

Privacy, confidentiality, and results

Any data or information (personal information) about you (including in reports, test results, images, samples or feedback) collected as a part of this research study will be stored securely as per UniSC's Research Data Management Procedures. All of your person information will be treated confidentially unless required by law. Data will be stored in a re-identifiable format.

Your de-identified personal information may be disclosed in reviews and reports arising out of the study which may be published. Your personal information and records relating to the study and any other information received about you will be kept strictly confidential and only shared in the below circumstances:

a) . b) Your referring doctor/s will be notified of your participation in this study and of any clinically relevant information noted by the trial doctor in the conduct of the study.
c) In the unlikely event that you are admitted to hospital following an adverse event resulting from this study, your treating doctor may require access to your study records.
d) Access may be required to your records for quality assurance, auditing and in the event of a serious adverse event.
e) If the government or legal authorities request any information or data relating to your individual participation in this study, or on the study in general, we are legally obliged to provide this information, and this may be without your consent.
f) If we believe that your life is in immediate danger, or the life of others is in danger, we are legally obliged to report this.

Once the study is complete and all data has been analysed, as referred to above the de-identified results may be published in peer-reviewed journals or presented at national or international scientific seminars and conferences. Research outcomes may also be shared with key authorities and community organisations so that the research findings can be realised in the wider community. If you wish to receive a copy of the overall results of the study, please contact the Chief Investigator (listed above).

Conflicts of interest
Dr Alain Brunet, Chief Investigator has been teaching reconsolidation therapy for a fee and is the Director of the not-for –profit Reconsolidation Therapy International Association (RTIA).

Funding
This project is internally funded by the Thompson Institute.

Agreeing to participate
Participation in this study is voluntary and you are under no obligation to consent. If you wish, you may take time to consider participating until you have discussed the decision with someone who is able to support you, such as a friend or family member. If you decide you wish to take part in the trial, you will be asked to sign the attached Participant Consent Form. By signing it you are telling us that you:

- Consent to take part in the study outlined above
- Consent to have the tests and treatments that are described above
- Consent for your data and information (personal information) to be collected in a re-identifiable format and used in analysis and publications in a non-identifiable format.
- Consent to the use of your data and information (personal information) for this study and any future research.

You will be given a signed and dated copy of this **Participant Information Form** and the **Participant Consent Form** to keep.

Withdrawing from the study
If you do decide to participate, you may withdraw at any time without any explanation or any penalty. You can withdraw your consent by advising the researcher verbally or via email or by completing and returning the **Participant Withdrawal of Consent Form** supplied herein. If you decide to withdraw from the study, you will have the choice whether to have your already collected data included in the analysis or not.

Respectful Behaviour
Thompson Institute as part of the University of the Sunshine Coast prides itself on providing a safe environment for staff, students and visitors. It is expected that the research team and participants treat each other with respect. Aggressive, abusive, threatening, discriminatory, or offensive behaviour or language will not be tolerated. If unacceptable behaviour occurs, we will take steps to reduce any detrimental impact of such behaviour, which may include research participation being immediately discontinued in the Thompson Institute's absolute discretion

Concerns or Complaints
If you have any concerns or complaints about the way this study is being conducted, you may raise them with the Chief Investigator (listed above). If you prefer an independent person, you may contact the Chair of the UniSC Human Research Ethics Committee: telephone +61 7 5430 2823; email humanethics@usc.edu.au).

Please save the information above if you choose to participate.

Consent to Participate in Research

Examining the biopsychosocial predictors of treatment response to propranolol-based reconsolidation therapy for trauma- and stressor-related disorders.

Ethics Approval Number: **XXXXXXX**

I have read and understood the above project information. I consent to participate and for my data and information to be used as described in the Project Information Consent Form and below.
I acknowledge and agree with the following:

- ☐ for this project and any future research
- ☐ I understand that I should not commence any new treatment/therapy whilst I am completing this research project.
- ☐ I consent to my treating doctor/s being notified of my participation in this study and of any clinically relevant information noted by the researchers in the conduct of the study.
- ☐ I understand the proposed treatment involves off-label use of propranolol facilitated by the study doctor.
- ☐ I understand that there are some instances where Thompson Institute research staff may be authorised or required under law to disclose my personal information without my consent, including to keep me and other people safe.
- ☐ I understand that participation in this research study does not replace any current treatment or therapeutic support I am receiving, and it is my responsibility to maintain contact with my existing treating team throughout the duration of the study. If it is found that I do not have a treating team at any point in the study, my participation in the study will be discontinued.
- ☐ I understand that my participation is voluntary. In signing this **Participant Consent Form**, I acknowledge that my consent to treatment can be withdrawn at any time, without giving any reason. Withdrawing from participation will have no effect on my medical care or legal rights.

Optional – These do not need to be checked to participate in the study

- ☐ I consent to the research team retaining my contact details so that I can be invited to participate in future related research.
- ☐ I consent to my treatment sessions being video recorded.
- ☐ I consent for any leftover biospecimens I have donated to the above study be used in future mental health research.

Personal / cultural preferences regarding biospecimens handling:

_____

_____

_____

Participant:

Name	Signature	Date

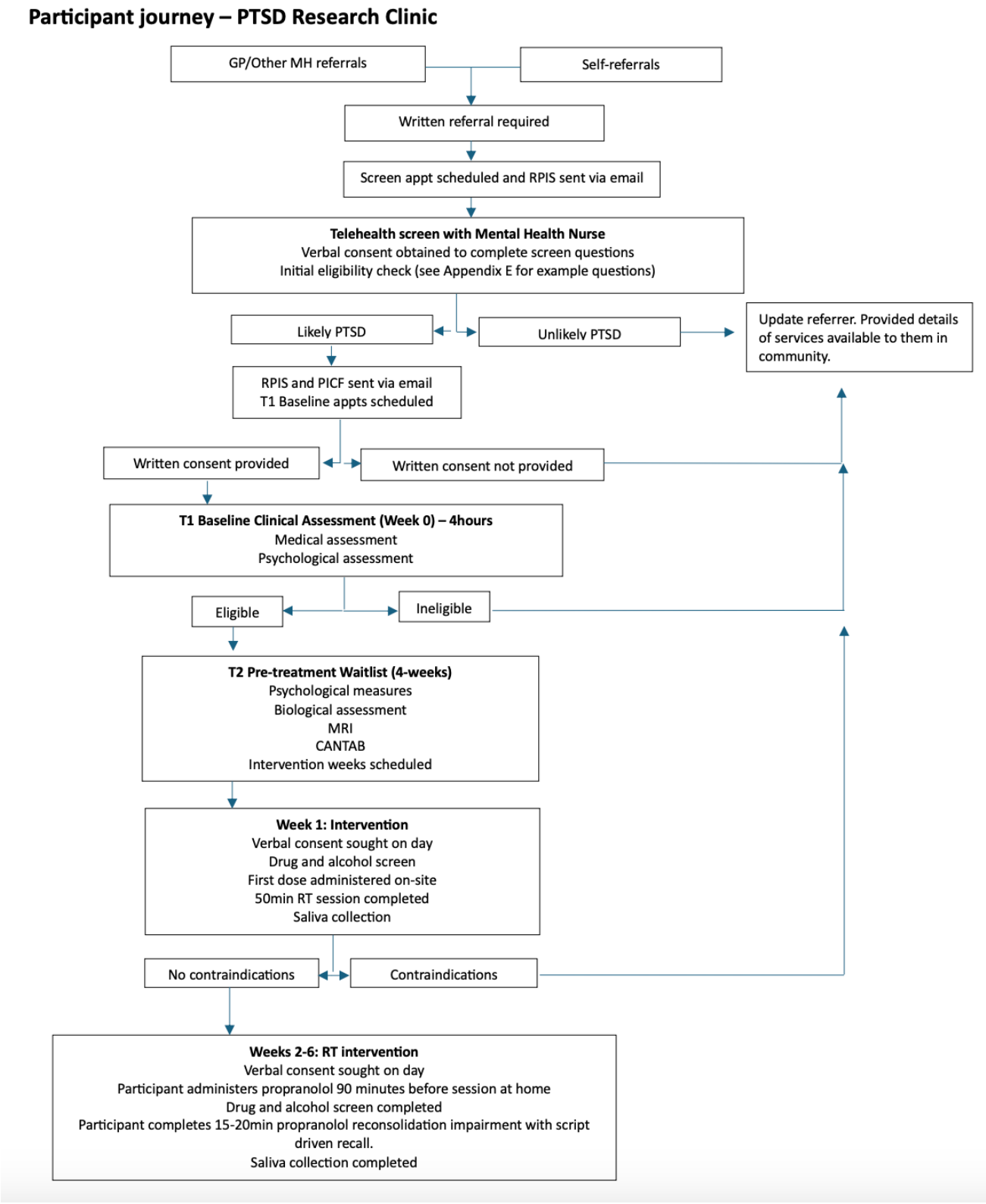
Witness:

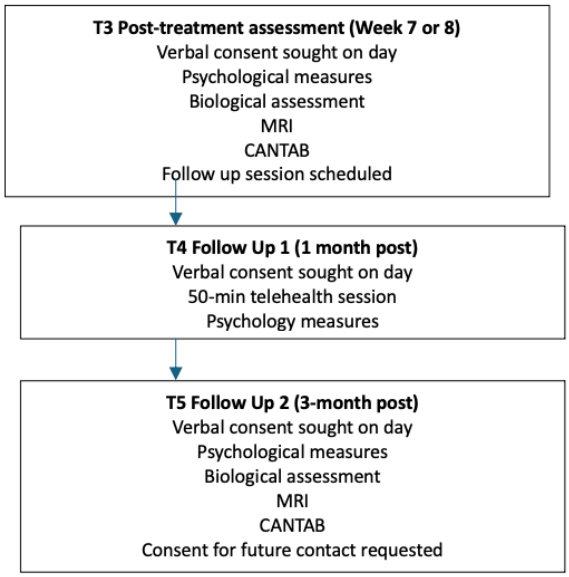
Name	Signature	Date

Declaration by Researcher:
I have given a verbal explanation of the research project; its procedures and risks and I believe that the participant has understood.

Name	Signature	Date

7.3 Appendix C. Visual flow of participant journey




T3 Post-treatment assessment (Week 7 or 8)
Verbal consent sought on day
Psychological measures
Biological assessment
MRI
CANTAB
Follow up session scheduled
T4 Follow Up 1 (1 month post)
Verbal consent sought on day
50-min telehealth session
Psychology measures
T5 Follow Up 2 (3-month post)
Verbal consent sought on day
Psychological measures
Biological assessment
MRI
CANTAB
Consent for future contact requested

7.4 Appendix D. Medical assessment

Measures	**Protocol and Key Questions**
Example physical health assessment questions	Study physician will perform a full physical examination including, but not limited to: Neurological system, cardiovascular system, Respiratory system, gastrointestinal system A 12-lead ECG will be performed Lying and standing blood pressure, as an active standing test • Participant is to be placed in a supine position, • Lying blood pressure is to be taken after being positioned supine for at least 5 minutes • The participant is to transition to a standing position • Standing blood pressure is to be taken immediately, then after 1 minute of standing. A participant will be excluded if there is a reduction in systolic blood pressure by ≥20 mmHg; a reduction in diastolic blood pressure by ≥ 10 mmHg or a heart rate increase of ≥ 30 beats per minute Heart rate variability using ECG rhythm strips. Drug and alcohol screen Significant medical history, past or present, including diagnosis, prognosis, and severity Medication the participant has taken in the last 3 months, including current regular medications: • Name: • Dosage: • Units: • Start date: • End date: • Use: Basal systolic blood pressure (exclude if <100mm Hg) Basal heart rate (exclude if <50 bpm) History of adverse reaction to a beta-blocker in the past (exclude if YES) Currently using a drug/substance that can interact adversely with propranolol? (exclude if YES) If this person pregnant or breastfeeding a child? (exclude if YES) Is this participant using contraceptives? (YES/NO/N/A) If yes, what type: Does this person present with a medical contraindication to take propranolol (exclude if YES): • Chronic obstructive asthma and bronchopneumopathy • Uncontrolled heart failure • Cardiogenic shock • Second- and third-degree atrioventricular block not paired • Spastic angina • Unpaired ear sinus disease • Bradycardia • Raynaud's syndrome and peripheral arterial disorders • Untreated pheochromocytoma • Arterial hypotension • Hypersensitivity to propranolol • Antecedent anaphylactic reaction • Hypoglycemia predisposition • Orthostatic hypotension • Other: Taking this all into account, can this person receive propranolol? (YES/NO) **Dosage and prescription of propranolol** Participants height: Determine the dosage using the table below:

Size (cm) Men	Size (cm) Women	Recommended dosage/propranolol session	Tablet (40mg)	Total number of tablets required
-	<1m55	40mg	1	8
<1m55	<1m65	50mg	1 ¼	10
<1m65	<1m75	60mg	1 ½	12
<1m75	<1m85	70mg	1 ¾	14
<1m85		80mg	2	16

Prescribe oral propranolol tables as per recommended dosage

- The number of pills is based on weekly treatment of 6 weeks
- Dosage should be taken with food 60min before the session

7.5 Appendix E. Psychological measures

Measures	Questions
Example telehealth screener interview questions	**Age Verification:** "To confirm, can I ask your age?" **Fluency and understanding of English:** "Are you fluent in English and able to understand the study information if it were presented to you in written format?" **Previous Trauma** "Without going into detail, what type of trauma have you experienced? (e.g., war, childhood, disaster) **Symptoms** "What symptoms do you experience?" **Previous diagnosis of PTSD:** "Have you been diagnosed with Post-Traumatic Stress Disorder (PTSD) by a healthcare professional previously?" **Current Treatment Team:** If yes, "do you have a current treating mental health team managing your PTSD or any other mental health conditions?" **Other Psychiatric Diagnoses:** "Have you ever been diagnosed with any of the following conditions?" Complex PTSD Psychosis Bipolar Disorder Personality Disorder Substance Use Disorder "What about other mental health diagnoses? Current or previously?" "Have you ever been hospitalised for your mental health?" **Medical History Related to Propranolol Use:** "Do you have any of the following medical conditions that might make propranolol unsuitable for you? This could include asthma, heart disease, very low blood pressure, or diabetes." **Allergies or Past Reactions:** "Have you ever had any adverse reactions to propranolol or similar medications in the past?" **Current Medications:** "Are you currently taking any medications that might interact with propranolol, such as other beta-blockers?" **Ability to Undergo Study Procedures:** "Would you be comfortable undergoing an MRI scan and participating in psychological and biological assessments as part of the study?" **Willingness to Participate:** "If eligible, would you be interested and willing to participate in this study and comply with the study procedures?" "Are you able to attend the Thompson Institute, 1 day per week for 6 weeks, with blocks of assessments on either side of this?"
Example pre-assessment pack questionnaires	**Peritraumatic distress inventory (PDI)** 0 = Not at All True; 1 = Slightly True; 2 = Somewhat True; 3 = Very True; and 4 = Extremely True. 1. I felt helpless 2. I felt sadness and grief 3. I felt frustrated or angry

Peritraumatic dissociative experiences questionnaire (PDEQ):
0 = Not at All True; 1 = Slightly True; 2 = Somewhat True; 3 = Very True; and 4 = Extremely True.

1. I had moments of losing track of what was going on – I "blanked out" or "spaced out" or in some way felt that I was not part of what was going on.
2. I found that I was on « automatic pilot » - I ended up doing things that I later realized I hadn't actively decided to do.
3. My sense of time changed – things seemed to be happening in slow motion.

PTSD Checklist for DSM-5 (PCL-5):
In the past week, how much were you bothered by:
(Not at all, A little bit, Moderately, Quite a bit, Extremely)

1. Repeated, disturbing, and unwanted memories of the stressful experience?
2. Repeated, disturbing dreams of the stressful experience?
3. Suddenly feeling or acting as if the stressful experience were actually happening again (as if you were actually back there reliving it)?

Beck Depression Inventory (BDI-I):
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Post-traumatic growth inventory (PTGI):
Indicate your score on a 6-point scale:
0 – I did not experience this as a result of my crisis.
1 – I experienced this change to a very small degree as a result of my crisis.
2 – I experienced this change to a small degree as a result of my crisis.
3 – I experienced this change to a moderate degree as a result of my crisis.
4 – I experienced this change to a great degree as a result of my crisis.
5 – I experienced this change to a very great degree as a result of my crisis

1. I changed my priorities about what is important in life.
2. I have a greater appreciation for the value of my own life.
3. I have developed new interests.

WHO Quality of life (WHOQOL):
0 = Not at all; 1 = Not much; 2 = Moderately; 3 = A great deal; and 4 = Completely.

1. Do you get the kind of support from others that you need?
2. How would you rate your quality of life?
3. How satisfied are you with your health?

The Impact of Event Scale – Revised (IES-R)
0 = Not at all; 1 = A little bit; 2 = Moderately; 3 = Quite a bit; and 4 = Extremely

1. Any reminder brought back feelings about it
2. I had trouble staying asleep
3. Other things kept making me think about it

Childhood Trauma Questionnaire (CTQ)
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International Trauma Questionnaires (ITQ)
0 = Not at all; 1 = A little bit; 2 = Moderately; 3 = Quite a bit; and 4 = Extremely

1. Having upsetting dreams that replay part of the experience or are clearly related to the experience?
2. Having powerful images or memories that sometimes come into your mind in which you feel the experience is happening again in the here and now?
3. Avoiding internal reminders of the experience (for example, thoughts, feelings, or physical sensations)?

Pittsburgh Sleep Quality Index (PSQI)
0= Not during the past month; 1=Less than one week; 2=once or twice per week; 3=Three or more times per week

	1. Cannot get to sleep in 30 minutes 2. Wake up in the middle of the night or early morning 3. Have to get up to use the bathroom
Example semi-structured and structured interview questions	**Structured interview:** 1. Mini international neuropsychiatric interview (MINI) **Semi-structured clinical interview: Under development.**

7.6 Appendix F. CANTAB assessment

Participants will complete the CANTAB computerised cognitive assessment battery in person at the Thompson Institute. This will be done in the presence of the researcher and will take approximately 30mins. The assessments will cover cognitive domains such as memory, information processing and speed as well as executive functioning. The CANTAB is a fully automated, self-administered neuropsychological test battery presented on an iPad. Once the participant details have been entered, the majority of instructions are delivered by CANTAB and the participant responds as instructed by the CANTAB. The researcher is required to verbally explain two subtests (Motor Screening Task and Rapid Visual Information Processing task) to participants. Other researcher involvement is rarely required, usually only to pause a test protocol should a participant require a rest break. Tests will include:

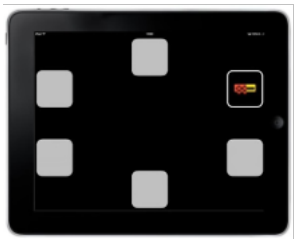
1. Motor screening task (MOT)
2. Paired associates learning (PAL)
4. Reaction time task (RTI)
5. Spatial working memory (SWM)
6. Rapid visual information processing (RVP)

*Motor Screening Task (MOT - CANTAB) – **Verbal explanation provided by research staff***

In addition to being a user-friendly way of introducing CANTAB tests to the participant, the Motor Screening Task provides a general assessment of whether sensorimotor deficits or lack of comprehension, will limit the collection of valid data from the participant. Administration time is 2minutes. Task format includes coloured crosses presented in different locations on the screen, one at a time. The participant must select the cross on the screen as quickly and accurately as possible. Outcome measures assess the participant's speed of response and the accuracy of pointing (selecting the cross).

Paired Associates Learning (PAL - CANTAB)

Paired Associates Learning assesses visual memory and new learning. Administration time is 8minutes. Task format includes boxes displayed on the screen and are “opened” in a randomised order. One or more of them will contain a pattern. The patterns are then displayed in the middle of the screen, one at a time and the participant must select the box in which the pattern was originally located. If the participant makes an error, the boxes are opened in sequence again to remind the participant of the locations of the patterns. Increased difficulty levels can be used to test high-functioning, healthy individuals. Outcome measures include the errors made by the participant, the number of trials required to locate the pattern(s) correctly, memory scores and stages completed.

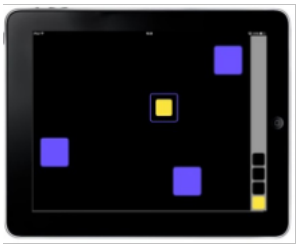


Reaction Time (RTI - CANTAB)

Reaction Time provides assessments of motor and mental response speeds, as well as measures of movement time, reaction time, response accuracy and impulsivity. Administration time is 3 minutes. Task format includes the participant selecting and holding a button at the bottom of the screen. Circles are presented above (one for the simple mode, and five for the five-choice mode.) In each case, a yellow dot will appear in one of the circles, and the participant must react as soon as possible, releasing the button at the bottom of the screen, and selecting the circle in which the dot appeared. Outcome measures are divided into reaction time and movement time for both the simple and five- choice variants.

Spatial Working Memory (SWM - CANTAB)

Spatial Working Memory requires retention and manipulation of visuospatial information. This self- ordered test has notable executive function demands and provides a measure of strategy as well as working memory errors. Administration time is 4 minutes. Task format includes beginning with a number of coloured squares (boxes) shown on the screen. The aim of this test is that by selecting the boxes and using a process of elimination, the participant should find one yellow 'token' in each of a number of boxes and use them to fill up an empty column on the right-hand side of the screen. Depending on the difficulty level used for this test, the number of boxes can be gradually increased until a maximum of 12 boxes are shown for the participants to search. The colour and position of the boxes used are changed from trial to trial to discourage the use of stereotyped search strategies. Outcome measures include errors (selecting boxes that have already been found to be empty and revisiting boxes which have already been found to contain a token) and strategy.



Rapid Visual Processing (RVP - CANTAB) - ***Verbal explanation provided by research staff***

Rapid Visual Information Processing is a measure of sustained attention. Administration time is 7 minutes. Task format includes a white box shown in the centre of the screen, inside which digits from 2 to 9 appear in a pseudo- random order, at the rate of 100 digits per minute. Participants are requested to detect target sequences of digits (for example, 2-4-6, 3-5-7, 4-6-8). When the participant sees the target sequence, they must respond by selecting the button in the centre of the screen as quickly as possible. The level of difficulty varies with either one- or three-target sequences that the participant must watch for at the same time. Outcome measures cover latency (speed of response), probability of false alarms and sensitivity


2
3 · 5 · 7

7.7. Appendix G. Propranolol indications, side effects and warnings

List of Beta-blockers	
Acebutolol	Sectral
Atenolol	Beta Adalat, Betatop, Tenordate, Tenoretic, Tenormin, Betanol.
Betaxolol	Betoptic, Kerlone
Bisoprolol	Monocor, Zebeta.
Carteolol	Carpilo, Carteol, Mikelan, Ocupress
Carvedilol	Coreg, Kredex
Celiprolol	Cardem, Selectol, Celipres, Celipro, Celol, Cordiax, Dilanorm
Esmolol	Brevibloc
Labetalol	Trandate, Normodyne
Levobunolol	Betagan, Ratio-Levobunolol
Metipranolol	Optipranolol
Metoprolol	Lopressor, Metoprolol Tartrate, Toprol.
Nadolol	Corgard
Nebivolol	Bystolic
Pindolol	Visken
Propranolol	Inderal, InnoPran XL, Hemangeol, Deralin.
Sotalol	Betapace, Sotylize.
Tertatolol	Artex, Artexal, Prenalex,
Timolol	Blocadren, Timolol Maleate-EX, Betimol, Istalol, Timoptic, Combigan, Digaol, Duotrav, Gaoptol, Nyogel, Nyolol, Moducren, Nyogel, Nyolol, Ophtim, Pilobloq, Timabak, Timocomod, Timoptol, Xalacom, Azarga, Cosopt, Dorzaolamide, Ganfort, Geltim, Timacor
List of drugs that may interact with propranolol	
Contraindicated	
Floctafenine	Floctafenine AA Pharma, Idarac
Sulpiride	Dogmatil, Bosnyl, Dogmil, Dolmatil, Eglonyl, Sulpitil, Sulpor, Sulparex, Meresa
Not Recommended	
Diltiazem	Cardizem, Cartia XT, Tiazac, Dilt-XR, Dilacorxr, Felodipine, Plendil
Verapamil	Calan, Isoptin, Verelan, Covera, Verapamil, Verap.
Fingolimod	Gilenya, Novartis
Precautions Required	
Amiodarone	Pacerone, Cordarone, Nexterone
Halogenated Volatile Anesthetics	
Antihypertensives (Central alpha agonists):	
Clonidine	Catapres, Jenloga, Kapvay
Guanfacine	Intuniv, Tenex.
Moxonidine	Physiotens
Rilmenidine	Albarel, Hyperium, Iterium, Tenaxum
Balcofen	Lioresal, Gablofen, Kemstro.
Ergotamine	Migergot, Ergomar, Cafergot
Fluvoxamine	Luvox
Insulin	
Hypoglycemic Sulfonamides	

Gilbornuride	Glutril
Glicalzide	Gliclazide, Diamicron
Glimepiride	Amaryl
Glipzide	Glucotrol
Lidocaine	
Medications that may lead to *Toursades de pointes*	
Antiarrhythmic drugs:	
Hydroquinidine	Termium, Dihydroquinine
Class III Antiarrhythmics:	
Dofetilide	Tikosyn
Ibutilide	Corvert
Sotalol	Betapace, Sorine, Sotylize.
Amiodarone	Pacerone, Cordarone
Neuroleptics	
Phenothiazines	
Cyamemazine	Tercian
Levomepromazine	Nozinan, Levoprome, Detenler, Hirnamin, Levotomin, Neurocil
Benzamides	
Amisulpride	Solian
Sulpiride	Dogmatil
Tiapride	Tiapridal
Butyrophenones	
Droperidol	Inapsine, Droleptan, Dridol, Xomolix, Innovar
Haloperidol	Haldol
Other Neuroleptics	
Pimozide	Orap
Other Medications	
Diphémanil Metilsulfate	Prantal
Erythromycin IV	Erythrocin
Halofantrine	Halfan
Methadone	Dolophine, Methadose.
Mizolastine	Elina, Zehist
Moxifloxacin	Avelox
Pentamidine	Pentam, Nebupent.
Spiramycin	Rovamycine
Vincamine	Oxybral SR,
Lumefantrine	Coartem
Propafenone	Rythmol
Rizatriptan	Maxalt
Medications to consider	
Urological Agents: increase hypotensive effect. Increases the risk of orthostatic hypotension	
Afulzosin	Uroxatral
Doxazosin	Cardura, Doxadura, Cascor, Carduran
Prazosin	Minipress

Tamsulosin	Flomax
Terazosin	Hytrin
Amifostine	Ethyol

- **Impramine (antidepressants, neuroleptics**): antihypertensive effect and increased risk of orthostatic hypotension (additive effect)
- **Alpha blocker Antihypertensive Drugs**: increases the hypotensive effect. Increased risk of orthostatic hypotension.
- **Dihydropyridines:** hypotension
- **Dipyridamole IV (Persantine)**
- **Phenobarbital (by extrapolation, primidone), Rifampicin (enzyme inducers):** decrease in propranolol plasma concentrations with reduced clinical effects (increased hepatic metabolism).

Most frequently reported:

- Asthenia
- Cooling of extremities; Raynaud's Syndrome
- Bradycardia
- Sleep disorders (insomnia, nightmares)
- Digestive disorders (gastralgia, nausea, vomiting, diarrhea

Rarely reported:

- **Reduced atrioventricular conduction or increased intensity of an existing atrioventricular block**
- **Heart failure**
- **Worsening of an existing intermittent claudication**
- Thrombocytopenia
- Severe drop in blood pressure
- Bronchospasm
- Hypoglycemia in at-risk patients (diabetes)
- Central nervous system disorders: hallucinations, psychosis, mood changes, confusion, impotence
- Paresthesias
- Various skin manifestations, including psoriasiform rashes

On a biological level:
In rare cases, the appearance of **antinuclear antibodies (ANA) has been observed, exceptionally accompanied by symptoms of Lupus Syndrome**, which resulted in the discontinuation of treatment.

Withdrawal of Consent

I, ... [PRINT NAME], wish to withdraw my consent to further involvement in research conducted at the PTSD Research Clinic at UniSC.

☐ I do not wish to continue participating in this research, but:
AGREE TO THE CONTINUED USE OF MY DEIDENTIFIED DATA ALREADY COLLECTED.

☐ I do not wish to continue participating in this research, and

I DO NOT AGREE TO THE CONTINUED USE OF MY DEIDENTIFIED DATA ALREADY COLLECTED.

Name: _____

Signature: _____

Date: _____

Name of Investigator: _____

Signature: _____

Date: _____

(UniSC Ethics approval XXXX)

7.10 Appendix I. Safety Measures Summary

Definitions

According to the ICH GCP E2 and E6 Guidelines, the definitions of adverse event and serious adverse event are:

Adverse event (AE)

Any untoward medical occurrence in a participant or clinical investigation participant administered a pharmaceutical product and which does not necessarily have a causal relationship with this treatment. An adverse event (AE) can therefore be any unfavourable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of an investigational product, whether or not related to the investigational product.

Serious adverse event (SAE)

Any untoward medical occurrence whether or not related to the investigational product that meets one of the six criteria:

- Results in death,
- Is life-threatening,
- Requires inpatient hospitalization or prolongation of existing hospitalization,
- Results in persistent or significant disability/incapacity,
- Is a congenital anomaly/birth defect,
- Is an important medical event requiring medical or surgical intervention to prevent serious outcome.

Suspected Unexpected Serious Adverse Reaction (SUSAR)

An event that is suspected as being related to the Investigational Product under investigation and is both serious and unexpected (the nature and severity of the event are not consistent with the information currently known about the medicinal product).

The National Cancer Institute Common Terminology Criteria (NCI CTC)

The National Cancer Institute Common Terminology Criteria for Adverse Events is a descriptive terminology which can be utilised for Adverse Event (AE) reporting.

AE and SAE Assessment

Causality

The causality of AEs (i.e., their relationship to intervention treatment) must be assessed by a suitable medically qualified Investigator at the Thompson Institute. Assessing causality requires considering whether there was a reasonable possibility that the event may have been caused by the intervention. In most cases, it is very difficult to categorically rule out a causal relationship. As such, the terms “related,” “possibly related” and “not related” will be interpreted as follows:

- “Related” – the reviewer is confident of the causal relationship (e.g. temporal association, existing safety knowledge of the product, clinical judgement);
- “Possibly related” – the reviewer is not confident of the causal relationship but tends to deem there is a positive causal relationship;
- “Not related” – the reviewer has no reason to believe there is a causal relationship at the time of the assessment (or tends to deem there is not a positive causal relationship).

Causality of an event may be re-evaluated by the reviewer at any time, e.g., when further evidence becomes available to confirm or refute an assessment of causality.

Severity

The Investigator will assess intensity for each AE and SAE reported during the study. The assessment will be based on the Investigator’s clinical judgement. The intensity of each AE and SAE recorded in the CRF should be assigned to one of the following categories:

- Mild: An event that is easily tolerated by the participant, causing minimal discomfort and not interfering with everyday activities or is considered mild by diagnosis.
- Moderate: An event that is sufficiently discomforting to interfere with normal everyday activities or is considered moderate by diagnosis.
- Severe: An event that prevents normal everyday activities or is considered severe by diagnosis.

An AE that is assessed as severe should not be confused with an SAE. Severity is a category utilised for rating the intensity of an event, and both Aes and SAEs can be assessed as severe. An event is defined as 'serious' when it meets one of the pre- defined outcomes as described in Section 10.1.

Recording of Adverse Events and Serious Adverse Events

Recording and reporting of an AE

All Aes will be documented on the case report form (CRF) or electronic CRF as per study requirements. The following types of information about the AE are commonly required:

1. Description of AE (a diagnosis is preferred);
2. Start date and end date;
3. Severity of the event;
4. Relationship to the investigational product;
5. Countermeasures;
6. Outcomes; and
7. Serious/non-serious.

The PI should try to establish a diagnosis of the event based on the signs and symptoms and/or other clinical information. If making a diagnosis is not possible, the PI will record the sign and/or symptom as an event.

1. The PI should follow the definition of the severity of adverse events as defined in the protocol.
2. The PI is required to assess the causal relationship between the IP and the AE.
3. The PI should ensure there is sufficient source data documentation to support the CRF entry.

Recording and reporting of a SAE

All the above procedures for recording and reporting of Aes also apply to that of SAEs. Any SAE that occurs during the study, whether related to trial treatment or not, must be reported by the PI within 24 hours after becoming aware of the event. The SAE is to be documented on the SAE reporting form contained in the individual case report form as stipulated in the protocol. The PI will document all available information regarding the SAE on the SAE reporting form. The initial SAE report should minimally include the following information or information otherwise specified in the protocol/study procedure manual:

1. Participant's study number;
2. Time and date of first starting the treatment;
3. Time and date of occurrence of the event;
4. A brief description of the event and countermeasures taken;
5. PI's opinion of the relationship with the IP.

The follow-up SAE report should be sent to the reporting bodies as soon as the follow-up information is available. The study site staff should follow the timeline for sending follow-up reports to sponsors, if any. The PI is responsible for complying with the requirements and reporting procedures of the HREC that granted approval of the study in relation to the reporting of SAEs. When preparing SAE reports to be submitted to the HREC, the study coordinator should ensure clear documentation of each specific report using the reporting procedure of the HREC that granted approval of the study. The PI is to manage any further action required by the HREC or regulatory body after reviewing the safety reports.

Handling in cases of Unresolved Aes and SAEs at completion or withdrawal

In the case of an AE or SAE, the participant will be appropriately referred and followed up with contact maintained until resolution or transfer of clinical care.

Procedures in case of medical emergency

All study staff members will receive medical emergency training, including CPR. The PI is responsible for ensuring all study staff members are aware of medical emergency procedures, and that there is relevant expertise available to manage medical emergencies at the study location. Medical emergencies will usually constitute an SAE and will be reported following the SAE reporting guidelines.

Within 24-48 hours of investigators receiving information that these events have occurred we will inform the HREC of the following:

- Any serious adverse events
- Any serious adverse drug reactions (ADRs)
- Any serious unexpected suspected adverse reactions (SUSARs)
- Any implemented amendments to protocol
- Any new safety information regarding oral ketamine use in published or unpublished studies relevant to the trial protocol.

We will submit **annual** reports to the HREC regarding:

- The progress of the study
- Any proposed amendments to protocol
- The secure maintenance of records and research data, and compliance with ethical conduct
- Upon **closure of the study**, we will inform the ethics committee and submit a closure report.

7.11. Appendix J. MRI Checklist

Thompson Institute

Magnetic Resonance Imaging (MRI) Consent Form and Safety Questionnaire

Full name: _____ **Height:** _____ cm

Date of birth (DD/MM/YYYY): ___ / ___ / _____ **Weight:** _____ kg

MRI Safety Questionnaire

Please ensure that you complete this questionnaire accurately. Your responses will assist in evaluating any risks associated with your MRI scan.

Do you have any of the following devices in/on your body?	Please tick
• Cardiac/heart pacemaker/pacing wires	☐ Yes ☐ No
• Implanted cardioverter defibrillator	☐ Yes ☐ No
• Artificial heart valve	☐ Yes ☐ No
• Implanted infusion or drug pump	☐ Yes ☐ No
• Electrical stimulator for nerves, brain, or bone	☐ Yes ☐ No
• Coils, filters, shunts, or stents	☐ Yes ☐ No
• Aneurysm clips	☐ Yes ☐ No
• Ocular (eye) implant	☐ Yes ☐ No
• Cochlear implant or other ear implant	☐ Yes ☐ No
• Mechanically or electronically activated implants	☐ Yes ☐ No
• Bullets, shrapnel, or other pieces of metal in your body	☐ Yes ☐ No
• Metal in your eyes (worked extensively with metal)	☐ Yes ☐ No
• Medicated skin patches (e.g., pain relief, hormone, nicotine replacement)	☐ Yes ☐ No
• Hearing aids	☐ Yes ☐ No
• Metal joints/joint replacement, pins, plates, rods, screws, nails, clips	☐ Yes ☐ No
• Tattoos/permanent tattooed makeup	☐ Yes ☐ No
• Body piercings	☐ Yes ☐ No
• Dental work (e.g. dentures, dental plate, braces, retainers)	☐ Yes ☐ No
• Metallic nail polish/make-up	☐ Yes ☐ No
• History of fits, blackout, epilepsy, or diabetes	☐ Yes ☐ No
• Surgical procedures or an endoscopy in the last 6 weeks	☐ Yes ☐ No
• Serious accident or injuries	☐ Yes ☐ No
• Possible or confirmed pregnancy	☐ Yes ☐ No
• Implanted contraceptive devices	☐ Yes ☐ No
• Are you wearing any clothes (including underwear), that contain metal wire, buttons or thread, or has been silver impregnated (e.g., anti-microbial)	☐ Yes ☐ No
Have you ever had any surgery? ***(If yes, please provide details below)***	☐ Yes ☐ No

Do you suffer from claustrophobia? ☐ Yes ☐ No ☐ Unsure ☐ Yes, but manageable

USC's Thompson Institute (USC) is collecting your personal information for the purposes of conducting research. Your personal information is handled in accordance with the *Information Privacy Act 2009* (Qld) and USC's *Information Management Framework – Governing Policy*. Unless authorised or required by law, we will not disclose your personal information to any third parties.

Magnetic Resonance Imaging (MRI) Consent Form and Safety Questionnaire

Preparing for your MRI scan

- You may be asked to change into a gown prior to your examination and your personal items will be stored securely.
- Do not bring anything into the MRI room with you. Some items brought into a magnetic field could result in harm to yourself, our staff, or damage the equipment, or the items themselves could be damaged or destroyed.
- Before your scan you must remove all metal objects in your possession or on your person.

Risks of an MRI scan

- Because ionising radiation is not used, there is no risk of exposure to radiation during an MRI scan.
- However, MRI uses very strong magnetic fields that are always on, and some objects pose a serious threat to safety. It is therefore vital that you answer the safety questions as accurately as possible, as some participants are unable to undergo an MRI.
- If you are pregnant, or suspect you may be pregnant, you should not proceed with the MRI, as it may increase the temperature of amniotic fluid.

Consent for an MRI scan

- I acknowledge that USC has explained the MRI scan procedure to me, and this form is accurate to the best of my knowledge.
- I have read and understood the safety questionnaire and have had the opportunity to ask questions about the MRI scan.
- I understand there are risks and complications associated with the MRI scan, including some risks that may be specific to me.
- I consent to undergoing the MRI scan.

Participant Details

Full Name: _____

Signature: _____ Date: _____

Parent/Guardian Details

Full Name: _____

Signature: _____ Date: _____

Office Use Only

I certify that I have screened this patient/participant and there are no contraindications to them entering the MRI scan room:

Study personnel name: _____ Signature: _____

Radiographer name: _____ Signature: _____

Date: __ __ / __ __ / __ __ __ __

Comments:

USC's Thompson Institute (USC) is collecting your personal information for the purposes of conducting research. Your personal information is handled in accordance with the *Information Privacy Act 2009* (Qld) and USC's *Information Management Framework – Governing Policy*. Unless authorised or required by law, we will not disclose your personal information to any third parties.

7.12 Appendix K. Recruitment Materials

Recruitment Email to Referral Network
Subject: Invitation to Participate in a Novel PTSD Treatment Study at UniSC's Thompson Institute

Dear [GP, Psychologist, Psychiatrist, Other Mental Health Professionals],

I hope this message finds you well. I am writing to inform you of an exciting new research study being conducted at the **National PTSD Research Centre** within **UniSC's Thompson Institute**. The Centre is focused on providing solutions for the 1.4 million Australians living with post-traumatic stress disorder (PTSD) and the many others impacted by psychological trauma.

We are currently recruiting participants for a study investigating an emerging treatment for PTSD, developed by the Thompson Institute's Director, **Professor Alain Brunet**. This novel treatment, known as **Reconsolidation Therapy**, has significant potential to improve lives by addressing the neurobiological mechanisms behind the brain's reconsolidation of traumatic memories.

Study Details:
- **Participants:** Adults aged 18 and over, with diagnosed or suspected PTSD
- **Duration:** A 6-week treatment intervention, with comprehensive assessments conducted before and after.
- **Intervention:** Reconsolidation therapy, which includes the use of a specific medication to temporarily make the brain more receptive to updating traumatic memories. The therapy itself is safe and non-invasive, and it doesn't alter consciousness.
- **Aims:**
    - To determine if a 6-session course of reconsolidation blockade treatment (i.e., oral propranolol treatment combined with script-driven trauma recall) is efficacious in reducing PTSD symptom frequency and severity in adults.
    - To examine the psychosocial, neurocognitive, neurobiological, neuroimaging and physiological effects of reconsolidation blockade treatment in adult participants with PTSD.
- **Eligibility:** A written referral from a medical professional is required for participation.
- **NOTE**: Participation in this study is not intended to replace existing treatment arrangements. Participants must have an active treating health team in place to be able to participate.

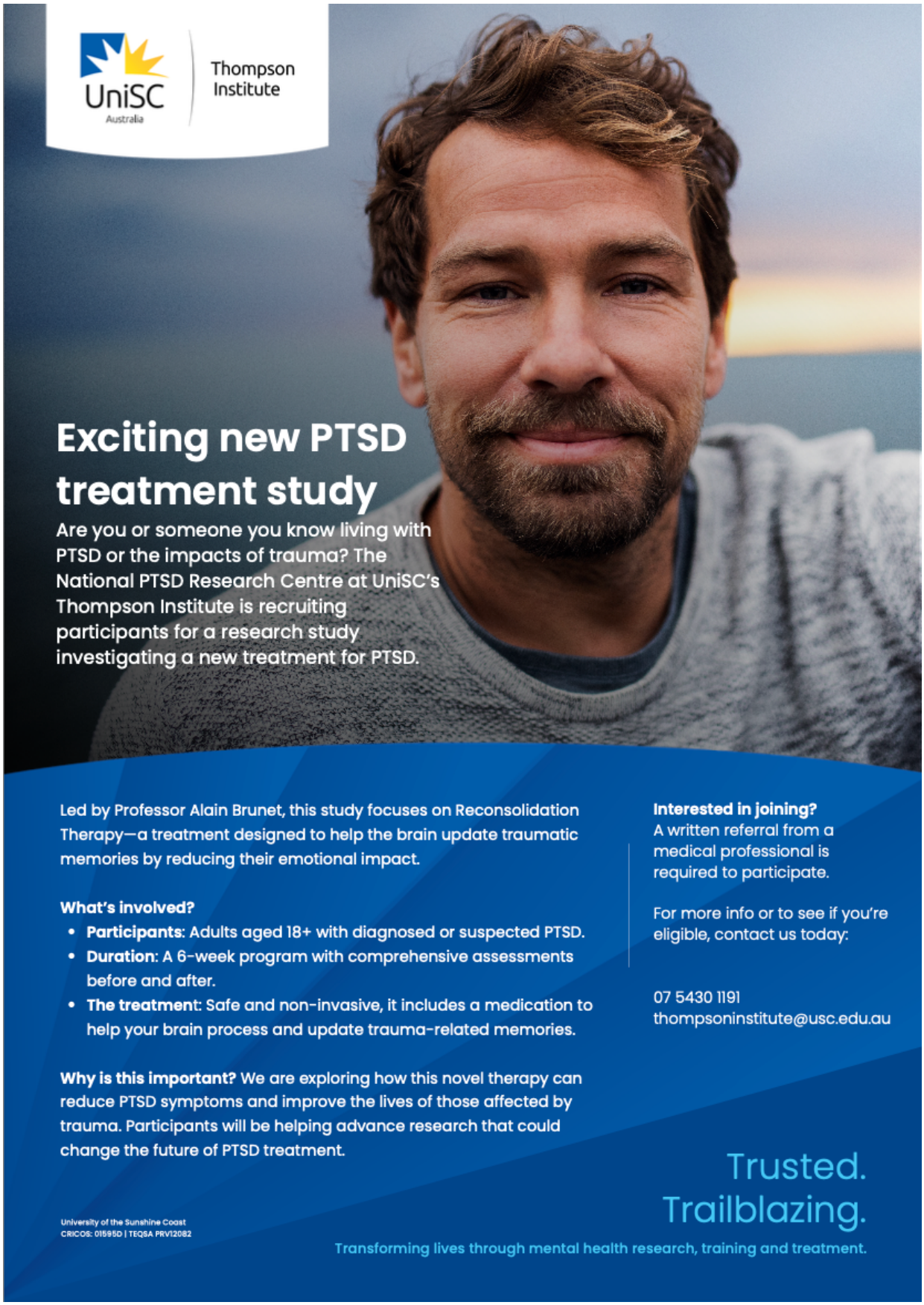
The study will be building on previous research on this topic and holds the potential to make a substantial difference in the lives of those affected by PTSD or trauma. If you have any patients who may benefit from this therapy, we encourage you to refer them to us.

For more information or to discuss the study in detail, please don't hesitate to contact us at thompsoninstitute@usc.edu.au. We look forward to collaborating with you in offering this innovative treatment option to those in need.

Kind regards

Trish Wilson
Manager, Clinical Programs
Thompson Institute National PTSD Research Centre
12 Innovation Parkway, Birtinya
University of the Sunshine Coast
Tel: +61 5456 3893
Mobile: 0412 105 399
twilson2@usc.edu.au | usc.edu.au

Recruitment Flyer



Social media post – Thompson Institute's Social Media Accounts
Exciting New PTSD Treatment Study at UniSC's Thompson Institute

Are you or someone you know living with PTSD or the impacts of trauma? The National PTSD Research Centre at UniSC's Thompson Institute is recruiting participants for a research study investigating a new treatment for PTSD.

Led by Professor Alain Brunet, this study focuses on Reconsolidation Therapy—a treatment designed to help the brain update traumatic memories by reducing their emotional impact.

What's involved?
- **Participants**: Adults aged 18+ with diagnosed or suspected PTSD.
- **Duration**: A 6-week program with comprehensive assessments before and after.
- **The treatment**: Safe and non-invasive, it includes a medication to help your brain process and update trauma-related memories.

Why is this important? We are exploring how this novel therapy can reduce PTSD symptoms and improve the lives of those affected by trauma. Participants will be helping advance research that could change the future of PTSD treatment.

Interested in joining the study? A written referral from a medical professional is required to participate.

For more info or to see if you're eligible, contact us today at thompsoninstitute@usc.edu.au.
Help us make a difference in PTSD treatment and share this post with someone who might benefit!

7.13 Appendix L. Risk Assessment Register

RISK REGISTER - Clinical Research Unit																	
User Display Code & last updated	Risk Description - current	Risk - caused by	Risk - Implications	Risk Category	Inherent Risk			Controls			Control Owner	Control Delegate	Residual Risk			Additional actions to be taken to mitigate Risk Treatment
TI_06	Danger, injury or harm to research participant or client	Interventions administered to patients as part of a clinical trial or research study, faulty or poorly maintained equipment, inadequate processes, poorly trained staff, aggrieved participant or client, exposure to traumatic events or recollection of experiences from participants or clients	Patient experiences negative or unexpected health issues and side effects, physical or psychological harm,disruption or discontinuation in trial or study, reputational impacts, legal impacts.	People Risk	Moderate	Possible	Medium	• UniSC ethics approval sought for all research studies • Informed written consent attained prior to commencement of study • Screening is undertaken of all participants • Trained technicians operating MRI • Ongoing MRI maintenance with external contractors • Standard Operating Procedures and Guidelines developed and maintained by Program Lead and subject matter experts; followed by all staff. • Program-specific processes have also been developed with review cycle in place • Staff are made aware of SOPs during induction and are supervised until competent • Ongoing training and professional development for clinicians and research staff • Swipe access to the building and 24/7 monitoring by SafeUniSC, 2 staff on site at all times with participants (including after hours) • Duress Alarms are fitted and in place and activated if there is any threat to staff or participant safety. Onsite safeUniSC staff respond during office hours with remote support provided by safeUniSC at Sippy Downs outside of normal working hours • UniSC EAP available for clinical debriefing sessions for staff • Debrief completed with all participants following Neurocognitive assessments to address any reported suicidality and/or distress observed or reported during the session • Suicidality escalation protocol and Distress Management Protocols developed and applied as needed • TI has client feedback processes in place for all consumers to provide compliments or raise concerns • Research team sends reminders to participants in the lead up to assessment days so that the participant can prepare • Call bell system with patient call button and staff assist button fitted and operational. SOP for staff re responses • Staff trained in clinical research practices, de-escalation skills, trauma-informed care, working alone and in isolation • All staff have completed GCP training • All clinical and neurophysiology assessments will be conducted within business hours, when clinical staff are accessible • Clinical support for RA's, to assist in managing participants and debriefing following assessments (when necessary)	Administrative	Effective	Director, Thompson Institute	Manager, Clinical Programs	Minor	Unlikely	Low	
TI_07	Danger, injury or harm to staff member, student or visitor	Staff member, student or visitor is injured by faulty equipment, other staff member, aggreived participant or visitor	Individual experiences negative or unexpected health issues and side effects, physical or psychological harm,disruption or discontinuation in trial or study, reputational impacts, legal impacts.	People Risk	Moderate	Possible	Medium	• Screening is undertaken of all participants • Standard Operating Procedures developed and maintained by Program Lead and subject matter experts; followed by all staff. • Program-specific processes have also been developed with review cycle in place • Staff are made aware of SOPs during induction and are supervised until competent • Ongoing training and professional development for clinicians and research staff • Swipe access to the building and 24/7 monitoring by SafeUniSC, 2 staff on site at all times with participants (including after hours) • Duress Alarms are activated if there is any threat to staff or participant safety. Onsite safeUniSC staff respond during office hours with remote support provided by safeUniSC at Sippy Downs outside of normal working hours • UniSC EAP available for clinical debriefing sessions for staff	Administrative	Effective	Director, Thompson Institute	Manager, Clinical Programs	Minor	Unlikely	Low	
TI_01	Breach of personal information	Accidental or willing breaches of private information, physical loss of data/records, cyber/network attack.	Privacy penalties, participant exposure, costs relating to remedying and notification of potentially affected parties, potential media attention, reputational impacts.	Regulatory and Compliance Risk	Moderate	Unlikely	Medium	• Hard copies of personal data is stored and locked away in cabinets in rooms with access restricted to key staff who are authorised to access the records. • Electronic records are stored in RealTime and the R drive with access restricted to authorised staff. Once data is entered into the system, it is de-identified and coded. Identifiable electronic data is only accessible to authorised staff with restricted access in accordance with the data management plan • Staff have individual logins to electronic participant software systems • Participant consent forms explain the limits of confidentiality if a participant is at risk of harm of self or others • Ongoing privacy training and professional development for clinicans and research staff • UniSC Policies and Procedures are in place in the event of a data breach. This includes, but is not limited to, recall of email, support from UniSC IT. Incident notification management and staff discussions. • UniSC has Research Data Management - Procedures in place • UniSC Information and Records Management Policy & Procedures in place. • UniSC Responsible Research Conduct - Academic Policy • UniSC Disposal of Digitised Records - Procedures. • UniSC Policies & Procedures include staff expectations in the management of the personal information of participants and clients • UniSC has mandatory training at induction with ongoing training and professional development for clinicans and research staff • Minimal identifying information is included in emails and does not include any sensitive information about the participant	Administrative	Effective	Director, Thompson Institute	Manager, Clinical Programs	Moderate	Rare	Low	
TI_08	Loss or damage to data and/or samples	Loss of power or service disruption, faulty or poorly maintained equipment, critical incident such as fire or flooding, procedures not followed.	Damage to equipment, project deliverables not met, leakage of helium into environment, damage to MRI, financial loss, reputational impacts.	Research Risk	Major	Possible	High	• Data will be stored in the cloud/data will backed up with secure process. Dual location of data storage will minimise risk of loss of data. Software selected to minimise loss of data due to technical failure (i.e. multiple save points or offline program/not dependent on power or internet). • Data management plan in place with UniSC that is reviewed on an annual basis • Power is maintained to the MRI at all times via backup generator • Trained technicians operating MRI • Ongoing MRI maintenance with external contractors • Standard Operating Procedures developed and maintained by Program Lead and subject matter experts; followed by all staff • Staff are made aware of SOPs during induction and are supervised until competent • SOPs are reviewed annually by Manager, Clinical Programs and relevant Thompson Institute Governance Committee/s • Ongoing training and professional development for clinicians and research staff	Administrative	Effective	Director, Thompson Institute	Manager, Clinical Programs	Moderate	Possible	Medium	UniSC Cybersecurity Risk acknowledged and managed by the Thompson Institute
TI_02	Breach of compliance obligations.	Not identifying a new regulation or a change in existing legislation, poor controls to comply with current legislation.	Penalty/s, legal action. Breach may also require HREC implications and further funding to Clinical Research programs	Regulatory and Compliance Risk	Major	Possible	High	• Regular liaison with UniSC on compliance with University expectations. • Annual reporting to HREC or as required • Restricted access to drug safe, and restricted access to drug room. • Restricted access to TMS machine. • Maintenance of drug register and audits of medication management procedures in accordance with Medicines and Poisons Act 2019 (Queensland) and Medicines and Poisongs Regulation 2021 (Queensland). • For participants that indicate suicidal intent during an assessment (e.g. telephone call; in-person), study protocol procedures and Thompson Institute Escalation of Care Guidelines will be followed and in consultation with the supervising clinician. Actions may include calling an ambulance in the case of an emergency. • Clinicians delivering treatment are registered through their respective registration board that is governed by AHPRA • Thompson Institute has an established Governance Committees that will retain oversight of clinical and research governance and compliance with legislation and guidelines.	Administrative	Effective	Director, Thompson Institute	Manager, Clinical Programs	Moderate	Rare	Medium	
RC_01	Inability to recruit a suitable amount and right demographic of research participants	Delays in relevant approvals (i.e. ethics, governance, contractors, other research partners) or barriers to participation	Unable to meet project outcomes. Inability to provide quality research that can be published in a well-respected journal. Further implications will limit future funding for ongoing research and will impact on the TI and UniSC reputation. Perception of inappropriate use of public or donated funds. Staff and students will decrease job satisfaction and may not be gainfully employed. Loss of PhD Students. Inability to gain reputational impact factors with regards to specialisations in Mental Health Research.	Research Risk	Major	Possible	High	• The TI NPRC has develped a recruitment plan prior to commencing operation and will amend this accordingly over the duration of the project • Projections and actuals spreadsheet commenced and updated by research team RAs to monitor actual recruitment and staffing needs • Adjust strategies if baseline drops below required intake per month • Engage and develop strong working relationships with stakeholders for recruitment and study related processes (e.g. GPs, Psychology practices, PHN commissioned services, mental health peer support groups) • Ensure participants understand the time commitment and expectations involved in participation, as well as any reimbursements/petrol vouchers. • Offer appointment SMS reminders if participants consent to this • When designing the project timeline allow for expected processing timeframes of external bodies and/or resubmissions (e.g. ethics or governance). • Allow flexibility where the protocol and approval bodies permit. • Ensure time and resources are delegated to ensure they are completed in timely manner. • Extensions requested in a timely manner if required. • Ensure adequate staffing is available to meet the intake/recruitment requirements. • Shared resources with other TI programs to meet intake/recruitment requirements. • Surveying of the local population and stakeholder networks to ensure appropriate intake/recruitment can be achieved.	Administrative	Effective	Director, Thompson Institute	Manager, Clinical Programs	Moderate	Possible	Medium	

RC_04	Biological hazards	Exposure to biological hazards from collection of pathology samples. Clinical staff are exposed to body fluids during the delivery of treatment and collection of biological samples.	Risk for transmission of infectious diseases	Research Risk	Moderate	Possible	Medium	• Staff appropriatly trained and qualified to undertake phlebotomy • Staff to follow standard and transmission based precautions, utilising supplied PPE, as required when conducting participant clinical assessments. • Sharps containers are located in prominent clinical areas • Biological hazard bins are located in clinical areas • Safety precautions and training for staff transporting blood to UniSC laboratories. • Staff/students/participants to be advised not to attend the Thompson Institute when they have signs & symptoms of illness or infection, including, but not limited to illnesses such as Influenza, COVID, and suspected gastroenteritis.	Personal Protective Equipment	Effective	Director, Thompson Institute	Manager, Clinical Programs	Minor	Rare	Low	
RC_05	Scheduling of assessments and interventions	Research participants require assessments and interventions as part of the research program. This includes time in dedicated clinical and research spaces that are used for other research and clinical programs at the TI	Assessments and interventions may not be completed within the allocated time frame, or completed at all due to competing priorities. Availability of space, access to medical equipment, availability of qualified staff to complete assessments and interventions, and availability of research participants may compromise this	Research Risk	Major	Possible	High	• A centralised booking system is available for the scheduling of MRI, EEGs and testing done in laboratories • The TI have developed Research Operations forums to discuss research throughput and long-term planning of research programs • Weekly research program meetings occur to discuss progress of clients through clinical assessments and interventions • Qualified clinicians and technicians are employed who can conduct assessments within an allocated appointment time	Administrative	Partially Effective	Director, Thompson Institute	Manager, Clinical Programs	Moderate	Possible	Medium	Require a mechanism that allows the monitoring in progress of research programs. To be discussed at the next Research Committee Meeting
RC_09	Negative health consequences to participants as a result of exposure to treatments	Drugs, medications and interventions administered to participants as part of the clinical trial.	Participant experiences negative or unexpected side effects, participant experiences negative health outcome (short or long-term), patient will not/cannot continue in trial, potential for UniSC reputation to be impacted	People Risk	Major	Possible	High	• Ethical approval and compliance throughout the trial process • Governance checklists and Operational Manual implemented and maintained. • NPRC clinical staff (medical officers and Registered Nurses) who are working with participants have completed and update-to-date CPR and anaphylaxis training. • Clinics to operate during business hours when SafeUniSC Officers are available to provide emergency response support, including advanced first aid. • Clinical elements of the trial (i.e. heart rate monitoring, psychiatric scales, screenings) will be conducted by clinical staff who have received clinical certifications (i.e. registered nurse, doctor) • Participants will undergo safety monitoring (i.e. physical assessments, suicidality monitoring) throughout the trial. • Participants will be withdrawn from the trial if they fall outside of the safety parameters • Rescue medication for client trial management available on site for administration by clinicians. • Emergency portable Oxygen available on site, in the clinic and with SafeUniSC officers. • AED available within the NPRC clinic.	Personal Protective Equipment	Effective	Director, Thompson Institute	Manager, Clinical Programs	Minor	Unlikely	Low	
RC_10	Participant does not attend or is late for allocated assessment procedure	Various reasons outside TI control including Failure to Attend, not wanting to attend appointment, bad traffic, personal factors	Researchers and rooms booked and no longer required, reschedule required, or loss of data for that time point if unable to reschedule	Research Risk	Moderate	Likely	Medium	• A protocol will be developed for managing cancellations including actions to take when a participant misses an appointment. • Contact participant to check in and reschedule appointment. • Participant will continue to be invited to future assessments unless they request to be withdrawn from the study or are outside of the the assessment timeframe outlined in the project protocol • Participants go through a screening process prior to the start of the study	Administrative	Effective	Director, Thompson Institute	Manager, Clinical Programs	Moderate	Unlikely	Medium	
RC_11	Access to restricted drugs is compromised	Lack of security, processes or staff error	Medico-legal implications, inability to deliver treatment/research medication, loss of control of restricted substance, legal implications, require contact to police	Research Risk	Moderate	Possible	Medium	• All Scheduled medications stored in accordance with the Medicines and Poisons Act 2019 (Queensland) the Medicines and Poisons Regulation 2021 (Queensland), and the Thompson Institute Substance Management Plan Regulated Medicines. •A drug register will be maintained and regular audits of compliance regulations will be conducted in accordance with thye Thompson Institute Substance Management Plan Regulated Poisons, Queensland legislation and regulations. The register will be stored in accordance with UniSC data safety policy and requirements of the Information Privacy Act 2009 - Queensland Legislation. • Any unused Investigational Product drug that is on-site at the end of the trial will be returned to the dispensing pharmacy for disposal.	Administrative	Effective	Director, Thompson Institute	Manager, Clinical Programs	Moderate	Possible	Medium	
RC_12	Participant requests continued access to Psychology Services or medicatoin on completion of trial	Perceived lack of effectiveness of trial treatment	Legal implications, medical implications in that ongoing treatment may be warranted, participant becomes dependant on trial staff and interventions	People Risk	Moderate	Likely	Medium	• If a participant wishes to continue using a trial drug, the participant is to be advised that this can be discussed with their treating medical practitioner or psychiatrist. • Reconsolidation therapy success cannot be guaranteed. A pathway to second and third-line treatments, such as EMDR, CBT can be offerred within the Clinic and/or referral to external mental health services for participants who do not benefit from Reconsolidation Therapy. • During the final Reconsolidation Therapy visit, the Clinical Psychologist/clinical team will discuss perceived benefit and options for follow up treatment with the participant. • Oversight of participants entering continued therapy following Reconsolidation Therapy is retained by the Clinical Governance Committee.	Administrative	Effective	Director, Thompson Institute	Manager, Clinical Programs	Moderate	Unlikely	Medium	Require a Risk Treatment Plan. This will be managed by the Data & Therapeutics Committee
RC_13	Participants' expectations of the treatment outcomes are not met	Limitations involved in conducting clinical trials	Reputation of Thompson Institute/UniSC can be impacted, affecting relationships in the community and future recruitment for clinical trials	Research Risk	Moderate	Possible	Medium	• Investigators will provide participants with a Participant Information and Consent Sheet (PICF) which will inform participants about the nature of the Reconsolidation Therapy clinical trial. This information will be confirmed verbally and in writing to participants prior to their commencement in the trial in accordance with procedures for obtaining informed consent. • Reconsolidation therapy success cannot be guaranteed. A pathway to second and third line treatments, such as EMDR and medication will be established for participants who do not report benefit from Reconsolidation Therapy. • During the final Reconsolidation Therapy visit, the Clinical Psychologist/clinical team will discuss perceived benefit and options for follow up treatment such as EMDR with the participant.	Administrative	Effective	Director, Thompson Institute	Manager, Clinical Programs	Moderate	Unlikely	Medium	
RC_14	Integrity of collected data is compromised.	An unauthorised person gaining access to data. Molecular biochemistry samples are compromised.	Integrity of the clinical trial is affected as data is compromised, reputation of Thompson Institute/UniSC can be impacted, affecting relationships in the community and future recruitment for clinical trials	Research Risk	Moderate	Possible	Medium	• SOP for pathology management is followed to ensure correct pathology collection procedures are followed and that blood samples can be analysed appropriately • TI procedures and research protocols followed by TI staff when completing pathology request forms for blood collection. • Research blood samples are collected and transported from in accordance with TI Management of Pathology SOP • Clinical blood samples (if required) are collected and processed by private laboratory service, with copies of reports sent to the clinical research team and the participant's general practitioner. • Research Pathology specimens stored in UniSC Lab which retains the integrity of the sample with oversight by TI Molecular Biologist (for quality control)	Administrative	Effective	Director, Thompson Institute	Manager, Clinical Programs	Moderate	Unlikely	Medium	
RC_15	Location of participant is unknown	Participant leaves the TI and does not arrive at the expected location	Participant may have been affected by the treatment delivered, unfamiliar to surroundings, or missing; leading to loss of a participant, compromise to their safety and reputational damage to the TI	People Risk	Moderate	Possible	Medium	• Contact details of participants and their Next of Kin are obtained at commencement of trial to ensure participants are well supported and an alternative person can be contacted in the event of an emergency • Participants are informed to return to their accomodation or residence upon completion of treatment • Participants that do not have someone to take them home or to their accomodation are provided a taxi voucher with Clinic staff ordering the taxi for the participant • Participants are observed for a minimum time period (as identified in the research protocol) before leaving the TI and may be kept for longer for observation if still under the effects to the treatment medication. The identified time period has clinical significance for the after-effects of treatment • Risk management plans are developed at the commencement of the study	Administrative	Effective	Director, Thompson Institute	Manager, Clinical Programs	Minor	Unlikely	Low	
TI_05	Fraud and corruption within the Thompson Institute	Staff spending money inappropriately, employment of contractors without due process, falsification of qualifications, falisification of research data, conflicts of interest and input into research for publications.	Financial loss, reputational impact regulatory scrutiny, fines, loss of confidence	Operational Risk	Major	Possible	High	• Financial approvals go through Institute Director and/or General Manager for review and sign off • Credit card limits in place and there is a monthly review of transactions • Responsible Officer Report from Finance reviewed by Institute Director and General Manager • Conflicts of interest - governing policy in place. • Limited staff have access to Taxi account & password • All staff complete mandatory GCP Research training. • Staff follow UniSC Responsible Academic Research Conduct - Academic Policy. • UniSC has a Compliance Management Framework in place. • UniSC has Fraud and Corruption Control Policy and procedures in place	Administrative	Effective	Director, Thompson Institute	Manager, Clinical Programs	Minor	Unlikely	Low	
TI_03	Loss of key staff	Key person risk, staff leaving and inadequate resources to continue research study or clinical trial, workforce retention issues. Staff absentism who are in critical roles and no backfil availbility	Continuation or delay of research study or clinical trial, disruption to operational functions, loss of continuity for participants and clients	Research Risk	Major	Possible	High	• Delegation of specific responsibilties and accountabilies in place • Executive and management team who regularly meet formally • Chief Investigator manages project specific procedures with relevant staff • Regular team meetings to share research issues and findings Succession planning and considerations include: • Opportunities provided to TI staff to step up into more senior positions or take on additional responsibilities, provided it is within their skills, knowledge and capacity • Ongoing recruitment of staff, including casual positions, to ensure minimal interruptions to business as usual due to staff absences. • Ongoing engagement with key stakeholders and community organisations in an attempt to recruit additional key roles at the TI	Administrative	Effective	Director, Thompson Institute	Manager, Clinical Programs	Major	Unlikely	Medium	

RC_21	Reputational Risk to the Thompson Institute and University of the Sunshine Coast	Ineffective delivery of Clinical Trials may lead to a poor perception of the Thompson Institute and/or the University of the Sunshine Coast	A poor reputation of the Thompson Institute or the University of the Sunshine Coast may lead to distrust of the community and a perception of poor use of public funds	Strategic/Growth Risk	Major	Unlikely	Medium	• Clinical Trials have been developed by a number of experienced researchers • All staff working the clinical trials have completed GCP • Regular team meetings occur to evaluate the program and ensure program deliverables are being met • All Staff are required to work within a defined Code of Conduct and in accordance with their professional responsibilities as a healthcare provider and/or employee of the University • Graded notification to respective managers and executives on potential threats to the reputation of the TI and/or UniSC • Standard Operating Procedures are in place to ensure staff are aware of responsibilities and processes in delivery of the program, providing a high quality program • Utilisation of TI Communications and Marketing to ensure a good reputation is being delivered across the community	Administrative	Effective	Director, Thompson Institute	Manager, Clinical Programs	Moderate	Rare	Low	

7.14. Appendix M. Recognising and Responding to Physiological Deterioration SOP

Recognising and responding to acute physiological deterioration – Operating Procedure

APPROVAL AUTHORITY
Director, Thompson Institute

RESPONSIBLE OFFICER
Manager Clinical Programs

DESIGNATED OFFICER
Medical Officer

START DATE
01 November 2024

LAST AMENDED
New Document

REVIEW DATE
01 November 2025

STATUS
Active

PURPOSE OF PROCEDURE

The early recognition and appropriate timely response to physiological deterioration is essential for ensuring safe and high-quality care at the Thompson Institute (TI).

The purpose of this document is to provide guidance for prompt and reliable recognition of and response to acute physiological deterioration in consumers who receive clinical treatments at the Thompson Institute.

SCOPE AND APPLICATION

This guideline provides guidance for clinicians and students who are working for the TI clinical services and/or clinical trials. The guidelines are to be utilised to support the early recognition and appropriate timely response to acute physiological deterioration of consumers who are receiving treatments at the Thompson Institute. Throughout this document, 'acute deterioration' refers to acute physiological deterioration. Deterioration in a person's mental state is covered in the TI 'Escalation of Care Guidelines'.

The Medical Officer has overall accountability for a consumer's care. Accountability for care also rests with other clinicians, including Registered nurses, and allied health professionals.

RELATED DOCUMENTS

- UniSC Medical Emergency Procedure
- UniSC TI Management of Clinical Incidents – Operating Procedure

RELATED LEGISLATION / STANDARDS

- Australian Commission on Safety and Quality in Health Care (2021) National Consensus statement: Essential elements for recognising and responding to acute physiological deterioration (third edition)

- Australian Commission on Safety and Quality in Health Care (2022) AS19/01: Recognising and Responding to Acute Deterioration Standard: Recognising deterioration in a person's mental state

DEFINITIONS

Please refer to the University's Glossary of Terms for policies and procedures. Terms and definitions identified below are specific to these procedures and are critical to its effectiveness:

Acute deterioration: Changes in the person's physiological or mental state that indicate a decline in the person's physical or mental health status
Adult Deterioration Detection System (ADDS) chart (or Track & Trigger tool): The standard observation chart [Appendix A] in use at the Thompson Institute NPRC for documenting and monitoring consumers vital sign observations. This tool enables the consumer's vital signs to be tracked over time and supports identification of changes in the consumers condition. (NSW Health, 2020)
Attending Medical Officer (AMO) / Nurse Practitioner (NP): The AMO or delegated NP has the primary delegated responsibility for the consumer receiving medical treatment.
Consumer: Refers to a person who is to receive clinical treatments in either the TI clinical services clinic, or clinic trials.
Clinician: 'A healthcare provider, trained as a health professional, including registered and nonregistered practitioners. Clinicians may provide care within a health service organisation as an employee, a contractor or a credentialed healthcare provider, or under other working arrangements. They include nurses, midwives, medical practitioners, allied health practitioners, technicians, scientists and other clinicians who provide health care, and students who provide health care under supervision.'(ACSQHC, 2021)
Orange Zone: The orange-coloured zone on the TI ADDs chart that represents warning signs of deterioration that requires an increase in the frequency of observations to 10-minute intervals, and review by the Nurse Practitioner or Medical Officer within 30mins.
Purple zone: The purple-coloured zone on the ADDS chart that represents warning signs of deterioration for which an emergency call response (Code Blue) is required.
Standard calling criteria: Signs and symptoms that a patient is deteriorating and requires medical review or escalation of care. Standard calling criteria are depicted on standard observation charts as yellow, red and purple zones. (NSW Health 2020)
Transfer of care: "The transfer of professional responsibility and accountability for some or all aspects of care for a consumer, or group of consumers, to another person or professional group on a temporary or permanent basis. Also known as clinical handover." (NSW Health, 2020)
Vital signs: 'Any objective parameter used to assess basic life functions.' (ACSQHC, 2021)

PROCEDURES

Clinical Process:

Measurement and documentation of vital signs and other observations

Regular measurement and documentation of vital signs is essential for recognising acute deterioration.(ACSQHC, 2021) Vital signs are to be monitored as part of physical assessments for consumers receiving treatments at the TI. To facilitate tracking of consumer's vital sign observations over time, observations are to be documented using the TI ADDS chart [Appendix A].

All consumers are to have baseline vital sign observations collected and documented at the time of their initial assessment, prior to commencing treatments, during treatment and after treatment in accordance with the specific treatment protocol. These observations are to include:

- respiratory rate,
- oxygen saturation,
- blood pressure,
- heart rate,
- temperature
- level of consciousness
- new onset of confusion or behaviour change

At the time of the initial assessment, baseline observations are to be documented on a TI ADDS chart. At this time, in addition to the observations listed above, the clinician conducting the initial assessment must also ensure that the following essential information is entered on the consumer's TI ADDS chart:

- the consumer's URN - Unique Record Number (Either their Healthcare record number, or RealTime reference number)
- the consumer's full name (first name and surname)
- the consumer's date of birth.
- The date and time the observations were recorded is also to be documented at the top of the respective column on the chart.
  Note: An exemplar illustrating the information required is provided in Appendix B.

Following the initial assessment, subsequent vital sign measurements are to be documented on the same ADDS chart, with the date and time the observations were recorded entered at the top of the column used to record the measurements.

When all columns of the ADDS chart have been used and a new chart is required, the consumer's baseline observation measurements and essential information (listed above) are to be transcribed onto the new ADDS chart. The completed ADDS chart is to be scanned and added to the consumer's electronic healthcare record. Research participants ADDS charts are to be scanned and filed in the participant's RealTime - Esource record. Once scanned, the hard copy is to be returned to the consumer's hard copy file.

Assessment of deterioration & escalation of care

The frequency of observations should be reconsidered when there are changes in the clinical observations that may indicate physiological deterioration.
The frequency of assessments will be increased when:

- the consumer's observations fall within a coloured zone (yellow, red, or purple) on the TI-Adds chart, OR
- other signs or symptoms of deterioration are identified (NSW Health)

Orange Zone: Clinical Review
Response:

- Any observation is in an orange area
- You are worried about the consumer, but they do not fit the orange zone criteria.

Actions required when observations fall within the Orange zone:

- Increase frequency of observations to 10 minute intervals
- Inform Nurse Practitioner or Medical Officer within 30 mins.
- Request review, and document notes on the back of the ADDS chart.
- Clinical notes regarding actions taken are to be documented in the consumers electronic record (Research Participant notes in RealTime eSource, consumers of clinical services to be documented in the electronic record or hard copy file used by the service).

Purple Zone: Emergency Call
Actions required when observations fall within the purple zone.
EMERGENCY CALL if:

- Any observation falls within the purple zone.
- You are worried about the consumer but they do not fit Purple zone criteria
- Begin initial life support interventions (support airway, breathing, circulation)
- Airway threat
- Respiratory or cardiac arrest
- New drop in O2 saturation <90%
- Sudden fall in level of consciousness
- Seizure
- You are seriously worried about the person but they do not fit the above criteria
- **Activate the Duress Alarm, Press Staff Assist Call Button, & Call 000** and follow the TI Emergency Response – Operational Procedures.

If an emergency call is initiated, after the emergency has been controlled and the consumer's care has been transferred to paramedics, the following must be completed:

- Clinical Incident report in OneVault in accordance with UniSC TI Management of Clinical Incidents – Operating Procedure.
- If the consumer is a participant in a clinical trial: Complete an Adverse event report located in the participant's RealTime eSource record.
- Detailed clinical notes documenting management of physiological deterioration to be completed in the Consumer's health care record or research RealTime eSource record.
- Medical summary to be documented and communicated with the consumer's primary treating team (GP and/or Psychiatrist).

7.15. Appendix N. Informed Consent Operating Procedure

APPROVAL AUTHORITY
Director, Thompson Institute

RESPONSIBLE OFFICER
Manager, Clinical Programs

DESIGNATED OFFICER
Quality & Risk Coordinator

START DATE
06/11/2024

LAST AMENDED
New Document

REVIEW DATE
Enter planned date

STATUS
Draft

PURPOSE OF PROCEDURE

This procedure outlines the procedure for Thompson Institute (TI) staff to follow when obtaining informed consent for consumers wish to receive treatments as part of TI clinical trials or clinical services.

Obtaining informed consent for healthcare procedures or treatments is essential for ensuring safe and high-quality care. Informed consent is a person's decision to voluntarily agree to a particular healthcare procedure or treatment. In accordance with the ICH Guideline for Good Clinical Practice and the Australian Charter of Health Care Rights, consumers have the right to clear, accurate and relevant information about the possible benefits and risks associated with different procedures or treatments, to enable them to make informed decisions when providing to consent for a healthcare procedure or treatment.[1,2.]

SCOPE AND APPLICATION

This operating procedure applies to all TI staff, students and contractors.

RELATED DOCUMENTS

- Consumer guide to the Australian Charter of Healthcare Rights
- UniSC Responsible Research Conduct Governing Policy
- Guide to Informed Decision-making in Healthcare; 2nd Edition

RELATED LEGISLATION / STANDARDS

- National Safety and Quality Health Service Standards 2nd Edition 2021
- Health Practitioner Regulation National Law (Queensland) - Queensland Legislation - Queensland Government
- Queensland Health Clinical Excellence Queensland, 2024 Guide to Informed Decision-making in Healthcare; 2nd Edition
- Australian Charter of Healthcare Rights | Australian Commission on Safety and Quality in Health Care

DEFINITIONS

Please refer to the University's Glossary of Terms for policies and procedures. Terms and definitions identified below are specific to these procedures and are critical to its effectiveness:

AHPRA: Australian Health Practitioner Regulation and Agency

Attending Medical Officer (AMO) / Nurse Practitioner (NP): The AMO or delegated NP has the primary delegated responsibility for the consumer receiving medical treatment.

Consumer: Refers to a participant/patient (their family and carers/legal guardian) who is to receive treatments as part of a TI clinical trial/clinical service.

Clinician: 'A healthcare provider, trained as a health professional, including registered and nonregistered practitioners. Clinicians may provide care within a health service organisation as an employee, a contractor or a credentialed healthcare provider, or under other working arrangements. They include nurses, midwives, medical practitioners, allied health practitioners, technicians, scientists and other clinicians who provide health care, and students who provide health care under supervision.'(ACSQHC, 2021)

Experienced: 'The health professional has the foundation of skills and knowledge to work appropriately to the position they are in and meets requirements one and two under Who can obtain informed consent?. The health professional is not considered a novice to the field/specialty and is not in a supernumerary position.'(QHealth, 2024)

Guardian: 'Means a person who is recognised in law as having the duties, powers, responsibilities and authority that, by law, parents have in relation to their children.' (QHealth, 2024)

Health care: Means the provision of a health service to diagnose, maintain, or treat the consumer's physical or mental health condition and is carried out by, or under direction of, a health provider. For example: Administering drugs or other substances, physical examinations, psychological assessments, treatment of mental illness, pathological or radiological investigations, clinical trials/medical research.

HREC: Human Research Ethics Committee

PICF: Participant Information and Consent Form

Procedures or Treatment: In the context of this document, means treatments or procedures that involve sedation, radiology, transcranial magnetic stimulation, and/or there are known risks or complications associated with the treatment or procedure.

Senior Health Professional: 'A health professional who meets requirement one to three under *who can obtain informed consent*'.[1]

Background

Types of consent

Implied consent: the consumer indicates their consent in their actions or willingly complying with the health care professional's instructions.[3] Implied consent is sufficient where the intervention does not present a significant risk to the consumer. For example, the consumer may give implied consent by extending their arm to have their blood pressure measured, or to allow the insertion of a needle for a blood test.[3]

Explicit or express consent: This can be given by the consumer either verbally, or in writing. Verbal consent occurs when the consumer verbally agrees to the health care.

Written consent, is where the consumer provided written evidence of their agreement to the health care. For written consent to be valid and informed, a signed consent form needs to be supported by appropriately specific and detailed information, which is either written on the consent form or documented in the consumer's clinical record/research record.[3]

PROCEDURE

Explicit written informed consent must be obtained from a consumer prior to the consumer engaging in a clinical trial or clinical service at the TI. It is important to understand that informed consent, requires more than a signature on the consent form. It is an interactive communication process for ensuring that the consumer had fully understood the

information about the benefits, risks and alternatives to the procedure or treatment that they are being asked to agree to.

When providing information for the consumer, the health practitioner should be frank and honest, be well balanced, be considerate when discussing potentially distressing information, and encourage two-way communication. Information should be communicated in simple, non-medical jargon terms, and when providing consent, the consumer should be able to demonstrate in their own terms, their understanding of the procedure or treatment that they are consenting to.

Who can obtain informed consent?

Informed consent for clinical procedure or treatment must be obtained by an experienced suitably qualified healthcare professional who:

1. Is able to competently provide the consumer with the necessary information about the health care procedure or treatment, including the risks, benefits, potential outcomes, complications and alternatives, so that the consumer can make an informed decision about the having the procedure or receiving the treatment.[1]
2. Registered with AHPRA in accordance with the Health Practitioner Regulation Law (Queensland).
3. Is credentialled to perform the health care procedure or treatment within their scope of practice (QHealth, 2024).

Delegated informed consent

A suitably qualified senior health care professional who meets the requirements stated above, may delegate informed consent to a Registered Nurse/Midwife, Nurse Practitioner, or Allied Health Practitioner. Delegation can occur on the condition that the delegate is supervised and supported by a suitably qualified senior health professional, and the delegate meets requirements one and two stated above.[1,3]
Where a senior health practitioner delegates consent,, they are responsible for:

- The decision to delegate the task and overall supervision of the delegate
- Ensuring that the delegate has necessary skills and knowledge of the health care to be provided to communicate with the consumer
- The delegate discloses the relevant information to the consumer consistent with the requirements for informed decision making.
- The delegate obtains and documents valid informed consent before care is provided to the consumer.[1,3.]

Obtaining informed consent

When obtaining written informed consent for TI Clinical trials or clinical services, the health professional must utilize the UniSC HREC approved PICF (participants) or UniSC approved consent form for clinical services which contain detailed written information about the clinical trial/service that the consumer is consenting to. It is not sufficient for the health professional to rely on the written material in the PICF/Consent form, they must also discuss the risks and benefits documented in the form and provide the consumer with an opportunity to have any questions or concerns addressed.[3]

Consent must be obtained, confirmed, and documented in accordance with the requirements in this operating procedure, the relevant research protocol or clinical service treatment protocol. It is also important to note that the consumer may withdraw consent at any given time, for any given reason, and withdrawal of consent can be done verbally or in writing.

Where a consumer lacks capacity to provide consent, a substitute decision maker (e.g., parent, legal guardian, Tribunal appointed guardian) may provide consent on behalf of the consumer. A consumer under 18 years of age, who is deemed by a suitably qualified health care professional as Gillick Competent, may provide consent for their procedure or treatment. However, if they are under 18 years of age and do not have capacity to give their own consent (not Gillick Competent) a parent or legal guardian may provide consent on the consumer's behalf.[1]

Documenting Informed Consent

A UniSC HREC approved TI PICF must be used for documenting consent for all research participants. Consent by consumers who are engaging in treatments provided by the TI Clinical Services must be documented using a consent form that has been approved by the UniSC legal services.

The consumer's consent form is to be stored in their relevant hard copy research file, or clinical services file. Research participants completed consent forms are to be scanned and uploaded to the participants electronic RealTime file. Clinical service consumers consent forms are to be scanned and uploaded to their electronic medical record.

If there are any changes in the risks or benefits of the health care treatment or options available, it is necessary to obtain a new consent. Otherwise, if there are no significant changes in the consumers health, the risks or treatment options available, informed consent for a particular procedure or treatment is considered valid for a maximum of 12 months if the following apply:

- Consent is for the same procedure/treatment
- The consumer is able to recall the information about the procedure/treatment risks, benefits, potential outcomes, complications and alternatives.
- The procedure/treatment risks, benefits, and alternatives have not changed
- There's no significant change in the intended outcome
- The consumer's health status has not changed
- The consumer has not withdrawn consent for the procedure/treatment
- There is no awareness of any new information that would impact the consumer's decision
- The substitute decision maker who provided consent on behalf of the consumer has not changed.
- The consumer maintains capacity to make informed decisions[1]

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