**Is there a synergistic effect of adding social cognition remediation to cognitive remediation therapy in young people? A randomised controlled trial**

1. **Aim**

Cognitive Remediation Therapy (CRT) and social cognition remediation (SCRT) are treatments that have evidence for their immediate efficacy in remediating the social and neurocognitive deficits of schizophrenia and other severe mental illness ([1-3](#_ENREF_1)). However, there is a paucity of information as to whether these treatments are effective for young people, whether the combination of these two treatment approaches is synergistic and if so, whether the combination’s effect is lasting and contributes to improved function and outcome. It is unclear which clinical group can best profit form the treatments. We propose a randomised controlled trial to address the following aims:-

1. Does a combined program of CRT and SCRT speed reintegration into work or educational?
2. Is there an advantage to combining these treatments over and above being treated by cognitive remediation alone?
3. Is there a clinical group that is particularly advantaged by combining CRT and SCRT?
4. **Background**

Outcomes for young people with a severe mental illness are still poor. Government pensions remain the main source of income for 85% of people with psychosis in Australia, with subsequent high rates of isolation and welfare dependency ([4](#_ENREF_4)). This has become a renewed focus for government with the announcement of a change in approach to young carers and welfare recipients as many have significant difficulties in returning to work or study because of the neurocognitive and social cognitive deficits that are part of their illness ([5-7](#_ENREF_5)). These deficits, at best, improve only minimally with current pharmacological interventions ([8](#_ENREF_8)) and until recently had no satisfactory treatment.

Neurocognitive (e.g., attention, concentration, memory, planning and speed of processing) and social cognitive deficits (emotion recognition, social cue perception, theory of mind, attribution, empathy) are basic components of psychiatric disease ([6](#_ENREF_6), [9-12](#_ENREF_9)). These domains, along with the negative symptoms of schizophrenia, are the major determinants of the longitudinal functional outcome and function ([6](#_ENREF_6), [13-15](#_ENREF_13)). These deficits are manifest before a person’s presentation to services with psychosis ([16](#_ENREF_16)), appear to worsen at the time of presentation and then stabilize to be chronic deficits ([17](#_ENREF_17)). A person who is unable to attend, remember, or plan their activities has great difficulty in functioning in a modern society which demands a rapid and complex response whether it is in a situation such as catching a bus requiring the ability to understand and work with bus timetables and money or within a work situation. Their ability to learn or integrate in a school or other learning environment is also severely affected. Further, without the ability to pick up upon social cues or appreciate the subtleties of social interactions people with cognitive and social cognitive deficits are significantly disadvantaged within social settings.

Recent advances in CRT and Social Cognitive Remediation

There is growing experience as to the effectiveness of specific treatments for neurocognitive and social cognitive deficits as adjuvant treatment to antipsychotic medication in schizophrenia and other severe mental illnesses. Two recent meta-analyses suggest that these therapies, can improve broadly based cognitive deficits with a moderate effect size, and on the basis of a subset of these studies, that these gains translate into improved community functioning ([1](#_ENREF_1), [18](#_ENREF_18)). Of particular interest are programs that combined CRT with other rehabilitation strategies such as vocational rehabilitation. This combined approach appears to best achieve these gains. Other predictors of improved functioning were the use of strategy approaches to cognitive remediation and youth. Two studies, our own ([19](#_ENREF_19)) and that of McGurk & Mueser ([20](#_ENREF_20)), suggest an advantage for younger people for this treatment. Our own study demonstrated improvements in attention, visual memory, cognitive flexibility, executive functioning and speed of processing after 10 weeks of computer assisted CRT. These changes persisted over the 4 months follow-up period and were associated with an improvement in community functioning ([21](#_ENREF_21)). There is evidence that the gain in cognitive function generalizes to other community activities, especially when integrated with other programs ([22](#_ENREF_22), [23](#_ENREF_23)).

The recognition of the existence and the parlous effect of social cognitive deficits has led to the development of social cognition remediation therapy ([2](#_ENREF_2)). The approach to the clinical problem has varied, but can be dichotomized into those programs that target and treat specific social cognitive deficits such as emotion recognition deficits ([24](#_ENREF_24)) or, alternatively, attempt to understand social situations and help develop the meta-cognitions required to understand the emotional world of another person ([25-27](#_ENREF_25)). Our research suggests that these improvements are significant and lasting ([28](#_ENREF_28)). Our own research in a group of people with chronic psychosis has demonstrated effective treatment for emotion recognition and deficits in empathic understanding and Theory of Mind deficits ([29](#_ENREF_29)).

Should CRT and SCRT combined required for maximal recovery?

The evidence that social cognition mediates the relationship between neurocognition and social functioning has had limited translation into treatment approaches. It is not clear whether impaired neurocognitive functioning ([9](#_ENREF_9)) might impede the ability of people with schizophrenia to benefit from social cognitive remediation. In our own work ([29](#_ENREF_29)), there was an interrelationship between baseline neurocognitive abilities and improved Theory of Mind (ToM) indicating that poorer working memory and lower IQ negatively impacted on the ability to benefit from SCRT training. This would support a contributory role of improved neurocognition to overall social cognition and outcome. This was consistent with our study of targeted emotion recognition training ([28](#_ENREF_28)), which also showed an effect of working memory on emotion recognition outcomes. We also need to know whether this has an impact of educational and vocational attainment, whether the treatment gets young people back into education or work. Thus, in this study we will directly test whether a treatment program comprising neurocognitive remediation before SCRT training is more effective than CRT alone.

1. **Research Plan**

The trial is a prospective single blind randomised controlled trial. We will recruit participants from mental health services in western Sydney (Cumberland, Blacktown, Prevention Early Intervention and Recovery Service, Youth Early Psychosis Program, headspace Parramatta & headspace Mt Druitt). The trial will compare the synergistic effect of combining Cognitive Remediation Therapy (using Neuropsychological Educational Approach to Remediation or NEAR ([30](#_ENREF_30))) with social cognitive remediation (using Social Cognition and Interaction Therapy (SCIT)([25](#_ENREF_25)) a manualised treatment against a control arm of NEAR + General Group Therapy.

Although funding has been attracted to pay for the neuropsychological and outcome testing the project needs the addition of specific therapists for both the CRT and SCIT groups. This will help in particular with the set up and running of the CRT and SCIT groups in the Blacktown/Mt Druitt areas where there has been no exposure to these treatments before.

Treatments

*Neuropsychological Educational Approach to Remediation (NEAR)* ([30](#_ENREF_30)) is a manualised CRT designed to address cognitive deficits by utilising commercially available educational software to create a rich learning environment that is intrinsically motivating and rewarding. The treatment will be provided over 10 weeks, 2 times per week to participants in groups of averaging 4 people. All patients will receive NEAR.

*Social Cognition and Interaction Therapy (SCIT)* ([25](#_ENREF_25)) is a manualised treatment designed to address social cognitive deficits. It consists of 20 one-hour sessions over 10 weeks. Training is run in small groups of three to six people using a manual-driven suite of activities. The training approach of SCIT is such that participants receive repeated exposure and practice of the skills that underlie complex mental-state reasoning abilities. Activities centre on social situations with a focus on making inferences and predictions about characters’ thoughts, feelings, and behaviours. Similar vignettes are repeated across different activities with frequent repetition of training material and concepts.

*General Group Therapy*. This will be a pragmatic construct used to balance the therapist time for each individual. Participants will be asked to attend another group activity at the centre. This could be made up of a wide range of activities including exercise, art therapy, relaxation or social skills groups. However, they will not be specifically aimed at improving cognition or social cognition.

Participants will be recruited in groups of 4 participants from a single location. After providing consent for involvement in the study all participants will complete the baseline assessment. All assessments will be conducted by research staff who will be blind to the group allocation of the individual participant and independent to the clinical team. The aim is to recruit a total of 80 young people over the 12 month period.

Treatment

**Arm 1:** *SCIT* = Participants randomised to this arm will be treated with 10 weeks of twice weekly of social cognitive remediation using the SCIT.

**Arm 2:** *General Group Therapy* = Participants randomised to this arm will be asked to attend any other group activity on a twice basis to balance the non-specific effects of exposure to a therapist time.

Participants will be randomised to one of two treatment arms on a 1:1 basis – Arm 1: SCIT; Arm 2: General Group Therapy. A randomised permuted block design will be generated independently of the researchers. The sequence will be placed in opaque envelopes and opened centrally by research staff not associated with participant assessment who will remain blind to allocation. Treatment will consist of 2 sessions per week of the interventions within the arm of the trial they have been allocated to for 20 weeks. Participants will be assessed at baseline, at the completion of treatment and 3 months after the completion of treatment.

Participant Inclusion and Exclusion criteria

**Inclusion criteria**: 1. A diagnosis of a severe mental illness and neurocognitive or social cognitive deficits); 2. Are aged 16-30 years; 3. Able to provide consent (and parent/guardian if required); 4. Have reasonable English skills.

**Exclusion criteria**: 1.Developmental delay (IQ < 75); 2.Current substance abuse or substance dependence other than caffeine or nicotine; 3. History of head injury (> 10 minutes unconsciousness). 4. Electroconvulsive Therapy in last six months.

Participants will be able to withdraw from the study at their own request, or if they suffer a significant deterioration in their clinical state in the opinion of the local chief investigator. A complete assessment will be attempted at the time of participant withdrawal.

Assessment

**Clinical**: Initial demographic and clinical details will be collected using a semi-structured interview that will detail age, duration of illness, age of onset of illness, treatment history, medication dose, years of education, past employment history, relationship history. Instruments used will include:

1. Simplified Negative and Positive Symptom Interview (SNAPSI); 2. Calgary Depression Scale (CDS); 3. Depression Anxiety and Stress Scale (DASS – 21) 4. Assessment of Quality of Life (AQoL-8D).

**Neuropsychological Function** will be assessed using a battery of neuropsychological measures to assess aspects of attention, concentration, vigilance, verbal learning, executive functioning, and premorbid intelligence – 1. Repeatable Battery for the Assessment of Neuropsychological Status (RBANS) 2. Trail Making Test A & B 3. Wechsler Abbreviated Scale of Intelligence II.

**Social Cognitive Function** will be assessed by measures of reading complex emotions, first and second order theory of mind, visual emotion processing and attributional style: 1. Hinting Task 2. Penn Emotion Recognition Task (ER-40) 3. Ambiguous Intentions Hostility Questionnaire (AIHW)

**Real World Functional Performance**: This will be measured by return to work or education and measures of functioning via the 1. Activity and Participation Questionnaire (APQ) 2. Social and Occupational Functioning Assessment Scale (SOFAS)

Analysis

The primary outcome will be real world performance. The secondary endpoints will include measures of neurocognitive and social cognitive performance, functional capacity, physical parameters and symptom profile. The multiple time points of measurement will assist in the assessment of mediating factors of the outcome. SCIT and CRT will be compared across 3 time points (baseline, End of Treatment, 6 months follow up) using using a repeated measures ANCOVA contrasting both within and between groups at three time points (baseline, end of treatment and six months). An effect size of 0.2 for the SCIT group and a power of 0.8. Given this a total sample size of 42 subjects is required to determine the result. This sample will be possible to recruit given the participant base of the youth mental health services that have agreed to join the project.

Adverse events

All adverse events will be reported to the WSLHD according to Good Clinical Practice. Although the treatments are inherently low risk they will be reviewed by the clinical team to check that no overall pattern is observable.

Significance and Outcomes

Early intervention in psychiatry was pioneered in Australia and has become a significant international service delivery priority. WSLHD was an early adapter of this clinical practice and the local teams have a strong record of research in this area. Early intervention has improved clinical outcome ([33](#_ENREF_33)) however these services have been developed without good intervention programs for cognitive deficits despite these being significant problems for these patients. Functional recovery from severe mental illness in young people is affected by both their illness and the interruption that they suffer to their educational and vocational progress due to admission and residual symptoms. Good treatment needs to focus on effective evidence based treatments that can reduce the cognitive deficits that are key to the development of this disability. We have previously shown that CRT works well for young people. At the end of this study we will have data that will indicate if combining CRT with SCRT provides a significant advantage to CRT alone in improving cognitive function and more importantly real-world functioning in young people with a severe mental illness. This will provide important information to structure community psychosocial treatment and provide pilot results for further work in this field (Strategic Plan 2).

Knowledge Translation plan

The project will help train new staff who have yet to be exposed to this treatment modality. This will be reinforced by the development of trainers in key facilities (PEIRS, BEAT and Redbank House) who will be able to train new staff in both CRT and SCIT. WSLHD staff are linked to other NSW Health areas via the Early Psychosis and Youth Mental Health networks. If the treatment trial is successful this will lead to joint training with other LHDs and the development of a broader trial of SCRT in this age group as was successfully done with CRT alone ([21](#_ENREF_21)). The chief investigator has been a key researcher in this field in Australia. The project will gather important pilot data about the use of SCIT in young people. This will be used in subsequent grant applications. The project will also involve clinical staff in a significant research project with an experienced clinical researcher, developing local capacity and helping to train our staff (Strategic plan 4).

More broadly the project will be used to demonstrate the importance of psychosocial treatments in severe mental illness. There has been an increasing reliance on medication in psychiatric treatment because of overwhelming unmet need in the community and the relative withdrawal from community psychiatry. The use of medication provides a foundation for treatment but reliance on medication alone does not provide for a good recovery. The demonstration of the ability of combined psychosocial treatment packages to return people with a severe mental illness to work and education at this early stage of illness is important not only for the individuals whose life course will be changed by the attainment of key educational and vocational goals, but for a system of care that is losing important treatment skills

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