Final report for Scientific Assessing Committee

Project title

Pilot RCT of Activation Therapy for Inpatient Depression

Health significance rationale

Depression is the most common reason for admission and readmission to mental health services within Canterbury and has high rates of associated disability which reflects national and international trends (Wells, Browne et al. 2006). Much of the disability associated with the disorder is due to impairment in important domains of cognitive and general functioning. Severe major depressive episode (MDE) often requires inpatient treatment, usually because of the risks associated with an inability to function at a level required for self care but also because of the strong correlation with suicidality. In inpatients with depression, cognitive deficits are larger and also fail to improve significantly with current treatment strategies (Reppermund, Zihl et al. 2007). Currently, patients continue to suffer significant cognitive impairment even when other depressive symptoms have resolved and this cognitive impairment is directly linked to impairment in other important domains of functioning (activities of daily living, occupational, interpersonal) (Jaeger, Berns et al. 2006). Evidence suggests that inpatient admissions do not adequately address the cognitive impairment that leads to readmission and on-going residual symptoms (Douglas, Porter et al. 2011). In Christchurch, between 2011 and 2015, approximately 300 patients per year were admitted to hospital with a primary diagnosis of major depression and following discharge 37% of patients were re-admitted to the inpatient unit within 12 weeks and a further 7% between 3 and 6 months. Our review of the evidence for the effectiveness of non-pharmacological interventions for acutely depressed inpatients (Crowe, Beaglehole et al. 2015) found that it was feasible and effective to deliver psychological/behavioural interventions in a busy inpatient setting. We subsequently developed a treatment package for severe depression in in-patients aimed at activation and in particular, rapidly improving cognitive function.

Research design

Pilot Study

This pilot study compared the effects of Activation Therapy (AT) with Treatment as Usual (TAU) for depression in a randomised controlled trial.

Novel Treatment – Activation Therapy

Based on the evidence and our experience with both psychological treatments and cognitive remediation for depression (Porter, Bowie et al. 2013; Porter, Douglas et al., 2014; Groves, Porter et al., 2015), we designed a combined therapy for inpatients with MDE– Activation Therapy (AT). This involves a combination of Behavioural Activation (BA) and cognitive activation (CA). The rationale for using a combined therapy was that patients in this study were severely depressed and it was unlikely that patients with severe MDE would be able to engage in CA without a BA component. The CA component involves a strategy of repeated cognitive exercise aiming to activate parts of the brain and the strategy of cognitive remediation using guided cognitive exercise and generalisation to daily life are different, but in our opinion exist on a spectrum.(Porter, Hammar et al. In press) The BA component is based on Lejuez et al.(Lejuez, Hopko et al. 2011) Personal values and activity preferences

are identified and activities focussed on this are selected using strategies of goalsetting, activity monitoring and scheduling of pleasant and mastery tasks. A hierarchy of graded task assignments are developed in collaboration with the therapist who also provides, close monitoring of progress and collaborative problem-solving of potential difficulties.

Methods
The purpose of the pilot study was to investigate the likely effect size differences of the two interventions and to refine the cognitive testing battery. The pilot study followed the same sampling, recruitment and intervention processes as the future larger-scale study.
Sample
Fifty inpatients aged 18-65 years with a primary DSM-5 (American Psychiatric Association 1994) diagnosis of major depressive episode (unipolar or bipolar) were recruited. Exclusions were minimal in order for the trial to be generalisable to all inpatients with depression and will be: primary diagnosis of schizophrenia or current severe drug or alcohol misuse, co-morbid serious endocrinological, neurological or chronic medical conditions, pregnancy, previous serious head injury, and electroconvulsive therapy (ECT) in the past 6 months. All patients were treated with pharmacotherapy as deemed appropriate by the treating multi-disciplinary team and randomised to receive additional AT or no additional therapy (TAU).

Key outcomes of the pilot study

1. Successful HRC project grant (1.2 million) to fund the larger definitive study.

   The HRC project grant commenced Oct 2018 and is scheduled to be completed Sept 2022. This will extend the initial sample of 50 participants (from this pilot study) to 170 participants across three sites (Canterbury DHB, South Canterbury DHB and Westcoast DHB). The grant from Canterbury Medical Research Foundation, allowed us to plan and cost the size of the definitive study and the need for 2 additional centres. The results of the total sample will be analysed together upon completion of the HRC project. Separate results for the pilot are not able to be completed as this would require us to break the blinding of randomisation. Interim safety analyses have been completed which did not identify any deterioration in mental health of participants.

2. Identification of Outcome measures for larger study

   The Initial proposal for the primary outcome in the larger study was change in cognitive functioning. Findings from the pilot study helped to identify that the most important outcome measure was rate of re-admission to hospital in the 12 weeks following discharge.

   The following outcome measures were also selected for the larger study: change in activity levels, cognitive function, general functioning and mood ratings between baseline and 14 weeks; re-admissions in the 1 year following discharge and days in hospital in the 1 year after baselin

3. Health system end user collaborations
   We have formed new research collaborations with a range of mental health services in Canterbury, South Canterbury and Westcoast DHBs

4. Contribution to developing the health research workforce through this research:
    1. Mereraina Porima is a Māori mental health nurse who recently completed her Masters of Health Science has.
    2. Zoe Barzyk, Doctoral student - Effects of Activation treatment on cognition in severely depressed