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Online neurocognitive remediation therapy to improve cognition in community-living individuals with a history of depression: A pilot study

Maria Semkovska*, Elayne Ahern

Department of Psychology, University of Limerick, Limerick, Ireland

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ABSTRACT

Major depression is a highly prevalent psychopathology with high relapse rates. Following remission from a depressive episode, neurocognitive difficulties in attention, working memory and executive function often persist, preventing full clinical recovery. These neurocognitive deficits are often present since the first depressive episode and have been shown to predict relapse. The efficacy of computerised neurocognitive remediation therapy (NCRT) to improve attention, memory and executive function has been demonstrated in several clinical populations but randomised controlled trials (RCT) have not been conducted in depression. The present study aimed to conduct a pilot, randomised study, of computerised NCRT for individuals with past depression, currently in remission. Twenty two individuals remitted from depression were randomly assigned to receive 20 one-hour sessions over 5 week of ether computerised NCRT or a component-equivalent allocation (play online computer games). The NCRT group showed significantly larger improvements in performance relative to the Games group in the three targeted neurocognitive domains: divided attention, verbal working memory, and planning, but also in non-targeted domains of long-term verbal memory and switching abilities. No significant effect was observed in the NCRT-targeted domain visual working memory. These preliminary results suggest computerised NCRT efficacy to improve targeted neurocognitive processes during depression remission and support its potential value as preventative connected intervention tool.

1. Introduction

Depression is the most prevalent mental disorder affecting about 13.5–21.2% of people during their lifetime (Hammar and Ardal, 2009). Direct costs to Europe represent 1% of its total economy and the overall depression burden is estimated at €118 billion (Sobocki et al., 2006). Depression is also the second largest cause globally for years lived with disability and the leading cause of disability for ages 15–39 (Vos et al., 2012). This substantial overall disease burden is further compounded by depression high relapse rates. After experiencing a first lifetime depressive episode, about 50 to 60% of people would develop a second episode (Beshai et al., 2011; Monroe and Harkness, 2011). The risk of depression relapse increases with each consecutive episode: about 70% relapse after a second episode and 90% relapse after a third episode. Estimated median of lifetime recurrence is 6 episodes with affected individuals spending about 21% of their life being depressed (Biesheuvel-Leliefeld et al., 2015). Recurring episodes are also associated with increasing risk of chronic depression, occurring when an episode does not remit for two years, and with an increased risk for dementia (Ownby et al., 2006).

Beyond mental and physical health issues, depression is associated with significant neurocognitive dysfunction. Numerous meta-analyses have demonstrated deficits in alertness, processing speed, sustained attention, memory and executive functioning (e.g., Ahern and Semkovska, 2017; Elderkin-Thompson et al., 2004; Rock et al., 2014). Empirical evidence further suggest that these neurocognitive deficits may worsen with repeated depressive episodes (e.g., Gorwood et al., 2008; Vanderhasselt and De Raedt, 2009), represent a significant predictor of relapse (e.g., Reppermund et al., 2009), and lead to reduced quality of life (e.g., Jaeger et al., 2006). Recent systematic reviews and meta-analyses show that, despite successful treatment (antidepressant medication and/or psychotherapy), these neurocognitive difficulties often persist following depression remission (Bora et al., 2013; Hasselbalch et al., 2011). Moreover, for some functions, this persistence of deficits following remission is already observable after recovery from a first episode of depression (Ahern and Semkovska, 2017). There is a growing consensus that neurocognitive impairment in depression cannot be fully explained by the presence or severity of mood symptoms (Bora et al., 2013; Rock et al., 2014). Therefore, improving neurocognition should be considered a key treatment goal

* Corresponding author.
E-mail address: maria.semkovska@ul.ie (M. Semkovska).

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while aiming at clinical remission, optimised recovery likelihood and relapse prevention. One such approach to therapeutically target these deficits is neurocognitive remediation therapy (NCRT).

NCRT involves the behavioural application of structured exercises with the aim of improving targeted neurocognitive processes (e.g., attention, memory) by mobilising brain plasticity that is the brain's ability to adjust its functions and connections in response to environmental change (Robertson and Murre, 1999). NCRT has demonstrated efficacy to remediate neurocognitive impairment in diverse groups of patients with neurological (e.g., for stroke, see Cicerone et al., 2011) or psychiatric conditions (e.g., for schizophrenia, see Wykes et al., 2011; for bipolar disorder, see Preiss et al., 2013). When computerised and non-computersied versions are compared, no significant differences in efficacy are usually found (e.g., Schoenberg et al., 2008; Wykes et al., 2011).

In the last ten years, several research groups have explored computerised NCRT for improving cognitive function in depression (e.g., Elgamal et al., 2007; Naismith et al., 2011). A recent systematic review and meta-analysis on the effect of computerised NCRT in depression (Motter et al., 2016) evaluated 9 studies and concluded that this intervention was associated with improved depressed mood, which could not be explained by concurrent treatment. Furthermore, this computerised intervention was associated with significantly improved daily functioning. Relatively to the targeted neurocognitive domains, attention and working memory improved significantly following computerised NCRT, while the small improvements in long-term memory and executive function did not reach statistical significance (Motter et al., 2016). The main meta-analysis's limitation consists in the high heterogeneity of the reviewed studies' design. More specifically, only five were randomised. From these, two studies (Calkins et al., 2015; Owens et al., 2013) were not using a clinical population with confirmed diagnosis (when this was the case for the remaining 7 meta-analysed studies), but a student population presenting with depressed mood as measured with the Beck Depression Inventory – II. One further study (Segrave et al., 2014) used concomitant transcranial direct current stimulation (tDCS). For the remaining two randomised studies, the control group was simply continuing receiving treatment as usual (Bowie et al., 2013; Siegle et al., 2014). Among the non-randomised observational studies, all four used waiting-list groups as a control condition (see Motter et al., 2016 for details).

To demonstrate robustly computerised NCRT efficacy, studies that are both randomised and use a “component-equivalent” control condition are essential. In fact, observed cognitive improvement following computerised NCRT, relative to a “no-cognitive-activity” control condition, can hypothetically be explained by the individual's engagement in mental activities, such as the memory and concentration required to perform computer games or for the interactions with the assisting therapist (Kurtz et al., 2007). Among the studies meta-analysed by Motter et al. (2016), only two were both randomised *and* used a “component-equivalent” control condition. However, as detailed above, these were conducted in non-representative samples of the general depression population, namely: students with low mood (Calkins et al., 2015) or patients treated concomitantly with tDCS (Segrave et al., 2014).

A recent randomised study in hospitalised patients with depression comparing computerised NCRT with a “component-equivalent” control, that is, playing computer games (Semkovska et al., 2015), partially supported Motter et al.' (2016) meta-analysis. More specifically, inpatients receiving 20 one-hour sessions of NCRT showed improved attention, working memory, long-term memory and planning abilities relative to inpatients involved in playing computer games for the same amount of time sessions, but both groups showed similar performance on other executive function measures. However, the improved neurocognitive performance in the NCRT group was not associated with the observed mood improvement and both groups showed equivalent depression severity decrease following the sessions' end. Here, we aimed to replicate the latter research methodology through a pilot study of patients recovered from depression completing the interventions online in the comfort of their home using the same research protocol as Semkovska et al. (2015). Although numerous effective options exist for treating depression during the acute stage, preventing depression relapse remains one of the biggest therapeutic challenges in the field (Monroe and Harkness, 2011). It is recognised that following successful therapy, depression relapse rates range from 50 to 80% once acute treatment is discontinued and 23–51% with continued treatment (Biesheuvel-Leliefeld et al., 2015). Given that neurocognitive difficulties are important predictors of depression relapse, target online NCRT could be helpful as adjunct to existing preventative therapies if reliably proven to improve targeted neurocognitive functions.

This study was planned and conducted according to recommendations for good practice in high quality randomised trial piloting design (Lancaster et al., 2004). It aimed to pilot the use of online NCRT as a connected intervention tool to improve cognition in community-living individuals with a history of at least one major depressive episode and survey participants' attitudes towards this intervention. Specific objectives were:

1. To collect feasibility data regarding recruitment rates, intervention adherence, retention rates and acceptance of randomisation in preparation for a full-scale randomised controlled rater-blinded trial assessing the effectiveness of online NCRT for improving cognition in recurrent depression;
2. To obtain preliminary data on the effectiveness of online NCRT as a connected intervention tool to improve targeted neurocognitive function (i.e., divided attention, working memory and planning);
3. To quantitatively explore participants' attitudes and expectations and experience relative to computerised NCRT as a connected intervention tool.
4. To compare the NCRT outcomes obtained in depression remitters to the results from Semkovska et al. (2015) obtained in inpatients treated for acute depression.

2. Methods

Recommendations for good practice in randomised trials piloting design (Lancaster et al., 2004) were followed for the development and analysis of the present research. Published guidelines for reporting the results of pilot investigation in preparation of RCTs using the Consolidated Standards of Reporting Trials were used (Thabane et al., 2010).

2.1. Participants and procedure

This pilot has received ethical approval from the Irish College of General Practitioners. Forty four local general practitioners (GPs) were contacted for participation in this pilot. Seven GPs agreed to participate. Based on our inclusion/exclusion criteria (see below), they referred, over a period of four months (17 weeks), 132 potentially eligible participants. More specifically, each GP referred patients who s/he has treated for depression in the past four years but who the GP now considered clinically remitted from depression. All 132 referred patients were approached to participate in the study through postal invitation containing the Information Sheet and 34 of them contacted us back. These 34 patients were assessed at the University of Limerick against the inclusion/exclusion criteria detailed below, Twenty two patients met the inclusion criteria and were randomised to receive either cNCRT (n = 11) or complete online computer games (n = 11) for 20 one-hour sessions. See flow-chart of recruitment in Fig. 1.

In terms of inclusion criteria, the study targeted community-living participants aged 18 to 65, with a past history of at least one major depressive episode (MDE) as confirmed with the Structured Clinical Interview for DSM-IV disorders (First et al., 1994), but currently in