2023-11-18

A pragmatic randomized controlled exploratory trial of the effectiveness of Eye Movement Desensitization and Reprocessing therapy for psychotic disorder

Rohit Shankar *Peninsula Medical School*

Simon Marlow *Cornwall Partnership NHS Foundation Trust*

Richard Laugharne *Cornwall Partnership NHS Foundation Trust*

Jon Allard

Paul Bassett *Statsconsultancy Ltd*

et al. *See next page for additional authors*

A pragmatic randomized controlled exploratory trial of the effectiveness of Eye Movement Desensitization and Reprocessing therapy for psychotic disorder

Marlow, Simon; Laugharne, Richard; Allard, Jon; Bassett, Paul; Priebe, Stefan; Ledger, Joanne; Kerr, Jacqueline; Priest, Deborah; Vanhoorn, Alje; Boland, Cailin; Shankar, Rohit

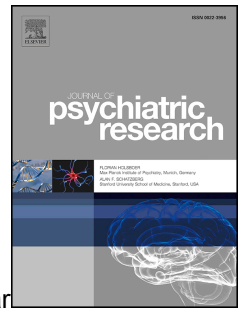
Published in:
Journal of Psychiatric Research

DOI:
10.1016/j.jpsychires.2023.11.024

Publication date:
2023

Document version:
Peer reviewed version

Journal Pre-proof



A pragmatic randomized controlled exploratory trial of the effectiveness of Eye Movement Desensitization and Reprocessing therapy for psychotic disorder

Simon Marlow, Richard Laugharne, Jon Allard, Paul Bassett, Stefan Priebe, Joanne Ledger, Jacqueline Kerr, Deborah Priest, Alje Vanhoorn, Cailin Boland, Rohit Shankar

PII: S0022-3956(23)00533-2

DOI: https://doi.org/10.1016/j.jpsychires.2023.11.024

Reference: PIAT 5935

To appear in: *Journal of Psychiatric Research*

Received Date: 11 March 2023

Revised Date: 4 November 2023

Accepted Date: 15 November 2023

Please cite this article as: Marlow S, Laugharne R, Allard J, Bassett P, Priebe S, Ledger J, Kerr J, Priest D, Vanhoorn A, Boland C, Shankar R, A pragmatic randomized controlled exploratory trial of the effectiveness of Eye Movement Desensitization and Reprocessing therapy for psychotic disorder, *Journal of Psychiatric Research* (2023), doi: https://doi.org/10.1016/j.jpsychires.2023.11.024.

A pragmatic randomized controlled exploratory trial of the effectiveness of Eye Movement Desensitization and Reprocessing therapy for psychotic disorder

Simon Marlow[1] , Richard Laugharne[1,2], Jon Allard[1], Paul Bassett[3], Stefan Priebe[4], Joanne Ledger[1], Jacqueline Kerr[1], Deborah Priest[1], Alje Vanhoorn[1], Cailin Boland[1], Rohit Shankar[1,2]*

[1]Cornwall Partnership NHS Foundation Trust, Truro, UK

[2]Cornwall Intellectual Disability Equitable Research (CIDER) University of Plymouth Peninsula School of Medicine, Truro, UK

[3]Statsconsultancy Ltd. Bucks UK

[4]Unit for Social and Community Psychiatry, Queen Mary's, University of London, UK

*Corresponding author: Professor Rohit Shankar MBE, FRCPsych, Threemilestone Industrial Estate, Truro, TR 4 9LD UK. Email address: rohit.shankar@plymouth.ac.uk

Short running title – EMDR and Psychosis

Word count – 3560 words

Disclosures- No author has any direct disclosure/conflict of interests related to the submitted work. RL has been chief investigator in studies for Janssen and Boehringer-Ingelheim Ltd. RS has received institutional and research support from LivaNova, UCB, Eisai, Veriton Pharma, Bial, Angelini, UnEEG and Jazz/GW pharma outside the submitted work. He holds grants from NIHR AI, SBRI and other funding bodies all outside this work. No other author has declared any conflict of interest.

Sponsorship and funding sources - None

Acknowledgements – Mrs. Deborah Marshall

Funding - The authors received no specific funding for this work.

Author Contributions- All authors satisfy the ICMJE guidance by substantially contributing to the design, analysis and interpretation of the work, drafting of the manuscript, final approval of the manuscript and all agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work is appropriately investigated and resolved.

Ethics -Full NHS and HRA Research ethics approval obtained for the study (REC ID - 15/SW/0034) and the study trial registered - ISRCTN43816889.

Abstract:

Background:

People with severe mental illness are often excluded from trials related to Eye Movement Desensitization and Reprocessing (EMDR) therapy. Principal concerns are that they may not tolerate treatment, might risk relapse or that psychotic symptoms may worsen. There is however building evidence of a traumatogenic etiology of psychotic disorder that may benefit therapeutically from EMDR. However, EMDR in this role is done mainly in specialist tertiary settings.

Aim:

To conduct a randomized exploratory trial of prospective treatment of EMDR for people with psychotic disorder and a history of trauma in an adult community mental health service.

Methods :

A randomized exploratory trial with a controlled pilot design was employed to conduct a prospective treatment and six-month follow-up study with an interim 10-week analysis in a rural county in the UK (population 538,000). We recruited participants with psychotic disorder who had a reported history of trauma and were interested in receiving trauma therapy. They were then randomized to either receive EMDR or treatment as usual (TAU). The primary instrument used was the Impact of Events Scale (IES) with secondary instruments of Positive and Negative Symptoms of Psychotic Disorder (PANSS), PTSD Checklist (PCL-C), and subjective Quality of Life (MANSA).

Results:

IES scores showed significant improvements in the EMDR group (n=24, age 42.0 SD (14.5), 42% male) compared to the TAU group (n=12, age 34.4 SD (11.3), 50% male) at 10 weeks and at six months ($p < 0.05$). There were significant improvements in PCL-C and PANSS negative symptoms scores associated with treatment ($p < 0.05$). All other scales showed positive trends.

Conclusions:

This study demonstrates that EMDR can reduce the impact of traumatic events for patients with a psychotic disorder in a clinical setting in the UK. The improvements in psychotic disorder persisted for six months after treatment.

Trial Registration: ISRCTN43816889.

Keywords: EMDR; Serious mental illness; Psychotic disorder; Psychotic Symptoms; Trauma

Introduction:

Trauma refers to experiences that cause a significant and intense psychological and physical stress response (Center for Substance Abuse Treatment 2014). Trauma is the lasting emotional consequence arising from living through a distressing event (The Centre for Addiction and Mental Health). Traumatic events could range from being single (e.g., assault, car crash, natural disaster etc.) to those of a long-term chronic pattern of negative impact (e.g., prolonged abuse or neglect etc.). They could be recent or in the past (e.g., childhood abuse). Experiencing a traumatic event can harm a person's sense of safety, sense of self, and ability to regulate emotions and navigate relationships. Traumatic experiences are related to psychotic disorders, and lead to impairments in social functioning, interpersonal relations and quality of life (Fares-Otero et al., 2023).

Severe mental illness such as psychotic disorders are commonly comorbid with Post Traumatic Stress Disorder (PTSD) and are also associated with poorer outcomes with respect to social and interpersonal functioning (Sin et al., 2017). Both pharmacological and psychological PTSD interventions for promoting recovery in psychotic disorders have been incorporated into national guidance (National Collaborating Centre for Mental Health, 2014).

There is evidence that trauma significantly increases the risk, severity and longevity of psychotic symptoms (Varese et al., 2012; Matheson et al., 2013). The potential for trauma-focused therapies to impact on both trauma-associated symptoms and other symptoms of psychotic disorder is well established (Brand et al., 2018; Sin et al., 2017b). Eye Movement Desensitization and Reprocessing (EMDR) therapy is recognized as an evidence-based psychotherapy for the treatment of PTSD (WHO, 2013). The evidence regarding the potential for EMDR to treat trauma-associated symptoms in other comorbid psychiatric conditions has led to support for its use in the treatment of psychotic disorder (Valiente-Gómez et al., 2017). The safety, tolerability and feasibility of EMDR as an intervention for people with psychotic disorder has been highlighted through recently published systematic and narrative reviews of research conducted (Adams et al., 2020; de Bont et al., 2019). EMDR evidence across studies indicate encouraging symptomatic benefits, including reduced negative symptoms and delusions related to psychotic disorder (de Bont et al., 2019; Laugharne et al., 2014; van den Berg et al., 2012). Early research indicates the potential for EMDR in treating psychotic symptoms even in the absence of definite comorbid PTSD (McGoldrick et al., 2008; Kim et al., 2010). A recent single-blind randomized clinical trial in China (n=57 total) found traumatic symptoms improved, psychotic symptoms reduced significantly and risk of developing psychotic disorder decreased when EMDR was used as an early intervention (Zhao et al., 2023).

The largest study to date is a multicenter, single-blind, six-month follow-up randomized control trial in the Netherlands, which found that patients with psychotic disorder in the EMDR arm (n=55) had reduced paranoid thoughts alongside increased remission from psychotic disorders post treatment (van den Berg et al., 2015; de Bont et al., 2016). Despite the growing evidence of EMDR for psychotic disorder, studies have primarily been conducted in specialist settings with limited evidence emerging from routine psychiatric services.

Aims:

We aimed to investigate if EMDR can reduce the impact of traumatic events for people with psychotic disorder who have a reported history of traumatic experiences in a routine clinical setting.

Our secondary aim was to explore if EMDR in this population reduces symptoms of psychotic disorder and PTSD and improves quality of life

Methods and materials:

The CONSORT guidelines to report Social and Psychological Interventions were used to guide the study reporting (supplementary information 1 and figure 1). We conducted a randomized exploratory trial. The study was of six months duration with repeated measurements at baseline, 10 weeks and 6 months. Participants were randomized to intervention and treatment as usual (TAU) groups. The intervention group were offered EMDR. The TAU group received standard care via the community mental health teams. All patients in the TAU group were offered EMDR at the end of the study period. Their EMDR intervention for the TAU group sat outside the study. There was planned unequal weighting toward the treatment group making it a pragmatic study with a ratio of 2:1.

Full NHS and HRA Research ethics approval was obtained by authors for the study (Research Ethics Committee ID - 15/SW/0034) and the study trial registered - ISRCTN43816889.
The study team recruited patients from community mental health services within Cornwall, a rural county in south-west England (population: 538,000). Cornwall has significant socio-economic deprivation and is 98% white-British in ethnicity.

Inclusion criteria

1. Patients aged between 18 and 64 receiving secondary mental health services with a diagnosis of either schizophrenia, bipolar disorder type 1 with psychotic symptoms, delusional disorder or schizoaffective disorder, irrespective of any other mental health comorbidities (including PTSD) using ICD-10 criteria (World Health Organization,1993).

2. Patients subjectively reporting traumatic experiences (not using semi-structured or standard interviews or questionnaires).

3. Patients expressing an interest in receiving trauma-focused therapy.

Exclusion criteria

1. Patients with insufficient competence of the English language

2. Patients with a significant intellectual impairment (IQ less than 70).

3. Patients unable to travel to assessments or therapy sessions.

4. Inpatients on a secure ward or patients deemed to be at significant risk or without the appropriate social support to engage in therapy.

The responsible psychiatrist approached eligible patients and provided them with information about the study and EMDR therapy. If they expressed an interest, an unblinded researcher arranged to meet with them and take consent. Blinded researchers completed baseline and follow-up assessments after receiving assessment tool training. Blinding to treatment allocation limited predictive or researcher bias.

Therapists offered participants in both groups up to eight sessions of EMDR within a 10-week intervention period, although the intervention was delivered to the treatment as usual TAU group after the end of their participation in the study. All study patients had TAU with respect to their psychiatric care, care-coordination, and offer of psychiatric medication. Therapists were psychiatrists and psychiatric nurses who had EMDR training (parts 1-4 of an EMDR Association accredited training program) who offered the standard protocol and had supervision arrangements in place with the lead researcher. There was no assessment of treatment fidelity due to limited resources available and to make the research practicable, given limited funding.

Case conceptualization consisted of standard approaches to find prior traumatic experiences that were associated with current difficulties. Therapists also considered case conceptualization guidance from the Netherlands (van den Berg et al., 2013). Patients may have received other psycho-social interventions such as CBT or family intervention approaches during the study period as part of TAU. Initial data collected included baseline demographics including age, sex, referral source, diagnosis and co-morbid substance misuse.

The number of EMDR sessions were identified through retrospective notes review completed by one of the authors with only those sessions recorded in patients' medical records included. Some patients in our dataset may therefore have had EMDR sessions not recorded in medical records.

Instruments

1. Impact of Events Scale – Revised (IES-R). The IES-R (Weiss and Marmar, 1997) is a reliable and validated assessment (Cronbach's alpha 0.95 and good reliability measures between 0,51 and 0.94) widely used across clinical populations, with scores >22 indicating post traumatic symptomatology (Creamer et al., 2003). This assesses amelioration of the present impact of traumatic events and includes subscales of symptom profiles of intrusion (IES-I), avoidance (IES-A) and hyperarousal (IES-H). IES scale has a total range of 0 to 88 with the IES-A and IES-I subscales having a maximum score of 32 each respectively and the IES-H having a maximum of 24.

2. Positive and Negative Symptoms of Schizophrenia Scale (PANSS) is a drug-sensitive rating instrument for schizophrenia (Kay et al., 1989, Kay et al., 1987) which includes subscales for balancing both positive (PANSS-P), negative (PANSS-N) symptoms along with general psychopathology (PANSS-G). The scale has excellent psychometric properties with Cronbach's

alpha at 0.70-0.85 and inter-rater reliabilities in the 0.80s (Kay et al., 1989) and is widely used in schizophrenia research to assess the current burden of psychotic disorder (Van den Oord et al., 2006). The total score has a range of 30-210 with the PANSS-P and PANSS-N subscales both having a range of 7-49 and PANSS-G subscale a range of 16-112.

3. PTSD Checklist– civilian (PCL-C). The psychometric properties of PCL-C are positive with a Cronbach's alpha of 0.90 and good reliability scores (Blanchard et al., 1996) with scores ranging from 17-85 assessing the burden of PTSD symptomology.

4. Subjective Quality of Life Scale - Manchester Short Assessment of Quality of Life (MANSA) is a short, reliable and valid quality of life assessment with a Cronbach's alpha between 0.75-0.84 (Priebe et al., 1999).
    1.

Outcomes

Primary outcome -

1. to assess the change in traumatic event impact on use of EMDR on people with psychotic disorder using IES-R.

Secondary outcomes -

1. Exploring the effect of EMDR on changes in general psychopathology, positive and negative symptoms of psychosis using PANSS.
2. The effect of EMDR on the core symptoms of PTSD measured by changes in the PCL-C.
3. Investigating the effect of EMDR on subjective quality of life measured by changes in the MANSA.

Statistical analysis:

The lead researcher independently completed randomization using a spreadsheet provided by a local university statistics department, which preserved blinding of other researchers involved, and he reminded participants to conceal their allocation status. Also blinded researchers had no part in any practical organization of therapy sessions and would not review medical records to be accidentally unblinded by seeing therapy notes. Blinded researchers had use of a research administrator who was not involved with the study to find or document information on the medical records.

Categorical variables are summarized by the number and percentage in each category, whilst the mean and standard deviation are reported for the continuous variables.

The primary analysis was based on repeated measures from baseline to follow-up measurement points at 10-weeks and 6-month follow-up. The analysis used Analysis of Covariance (ANCOVA) with the outcome variable being the measurement at 10-weeks or 6-month follow-up, and the equivalent baseline measurement included as a covariate. The effect of the intervention on repeated measures was estimated as a mean difference in outcome between groups with a 95% confidence interval. Cohen's d was also calculated as measure of standardized effect size, with significance accepted at $p< 0.05$. The assumptions of the analyses were checked for all

outcomes. All residuals were found to be normally distributed, and there was no pattern between the residuals and predicted values. An intention to treat analysis was not conducted. A post-hoc sample size calculation was performed based on the primary of the IES score at 10-weeks. A comparison of the amount of missing data in the two groups was made using Fisher's exact test, due to relatively small number of missing values.

Results:

The study involved 36 patients with 24 randomized to the treatment arm (mean age 42 years SD 14.5, male 42%) and 12 to the TAU arm (mean age 34.4 years SD 11.3, male 50%). One patient was recruited to the study but is not included in the 36 participants as they withdrew consent before the study began.

For the 36 patients, two provided no baseline data (one in each group) and two patients provided incomplete data (both in the intervention group) (**Table 1**).

Two were randomized to the EMDR arm but did not commence treatment and withdrew themselves from the study. Their data is included in the baseline data (**table 1**), but they are the two subjects missing from the follow-up data both at 10-weeks and at 6-months.

The sociodemographic and baseline scores on outcome measures of participants are shown in **Table 1**. There were no significant demographic differences between the two groups.

The mean number of EMDR sessions completed in the intervention arm of the study was 4.6. The mean number of sessions for the nineteen patients in the intervention arm who we have follow-up data for was 5.1. None of the twenty-two patients randomized to the EMDR treatment arm who commenced treatment explicitly withdrew from EMDR intervention.

There were patients lost to follow up. At 10-weeks 19/24 patients in the EMDR treatment arm were interviewed and 8/12 patients in the TAU arm, i.e., 9/36 patients were not available for interview at this time (10 weeks).

At 6-months, 17/24 patients in the EMDR treatment arm were interviewed and 10/12 patients in the TAU arm i.e., 9/36 patients were not available for interview. There were two subjects in TAU who were not interviewed at 10-weeks but interviewed at 6-months, and two subjects lost to follow-up after being interviewed at 10-weeks.

Outcomes at 10 weeks

Study outcomes at the completion of treatment at 10 weeks are shown in **Table 2**. There is an improvement in the primary outcome measure associated with EMDR treatment compared with TAU. The effect size for analysis of the total IES score was 1.49 (p = 0.03) with a clinically sig-

nificant mean difference of 21 units on the scale. The 10-week results suggest that the improvement in the IES scale is most associated with an improvement in the intrusion subscale (p = 0.03) as other subscales did not reach significance.

PCL-C scores also fell more in the EMDR group with an effect size of 1.36 (p = 0.02) with a clinically significant mean difference of nearly 15 units on this scale. No significant differences between groups were observed for the PANSS (and its subdomains) and the MANSA.

Six-month outcomes

A similar set of analyses were performed for outcomes at 6-months and are presented in **Table 3**. Comparing with TAU there is an improvement in the primary outcome measure associated with EMDR treatment. The effect size for analysis of the total IES score was 1.22 (p = 0.04) with a clinically significant mean difference of 17 units on the scale. The 6-month results suggest that the improvement in the IES scale is most associated with an improvement in the hyperarousal subscale (p = 0.03) as other subscales did not reach significance.

The PCL-C scores did not significantly improve in association with treatment though this was close to significance (p = 0.06) with an effect size of 1.15. No significant differences between groups were observed for the MANSA. Improvements in the PANSS score associated with treatment did not reach significance with an effect size of 0.67 (p = 0.09) however there was a significant drop in the negative symptom subscale of PANSS associated with treatment (p = 0.03).

The post-hoc analysis assumed a mean difference of 2.9 units between groups (based on the ANCOVA analysis), and assuming standard deviations of 1.7 and 3.7 in the two groups. Additionally, in line with the analysis method, the correlation between the baseline and 10-week scores was also factored into the calculation. The size of the correlation was assumed to be 0.36, as observed in the current data. Using a 5% significance level, an 80% power and a ratio of 2:1 in the two groups it is calculated that 8 and 16 subjects in the TAU and EMDR groups respectively would be required for the study. This is a roughly equivalent number to that included in the study. No adverse events linked directly or indirectly were noted.

Four of 12 (33%) in TAU group and five of 24 (21%) of the EMDR group had missing values at the end of treatment. The amount of missing data was not significantly different between groups (p = 0.44, Fisher's exact test). At the end of six-month follow-up, the TAU group had two of twelve and the EMDR group seven of twenty four with missing data. The amount of missing data was not significantly different between groups (p = 0.69, Fisher's exact test)

Discussion:

This pragmatic exploratory randomized controlled trial of EMDR for patients with a psychotic disorder reporting traumatic experiences demonstrated a benefit of therapy compared to treatment as usual on the primary outcome measure, the IES, at 10 weeks which was sustained at 6

months post treatment. There were also improvements in the PCL-C at 10-weeks, indicating the primary outcome effect may correlate with the effective treatment of comorbid PTSD or sub-syndromal PTSD symptomology. These findings are encouraging especially given the number of patients in each group was small. The study was delivered in a standard service in the UK National Health Service rather than a specialist facility, suggesting this research can be relevant for routine services but might require more testing.

Positive results were also noted in patients receiving significantly fewer than the offered eight sessions of treatment. Where this occurred, patients either missed booked sessions or agreed with their therapist that they had tackled all identified targets in their case formulation using the standard protocol. Whilst this meant patients attended less than the protocolized eight sessions, it also suggests EMDR could be effective for some people when a flexible approach is offered as is common in the UK community mental health care.

The effect on negative psychotic symptoms at six months while encouraging is hard to interpret or draw any conclusions from this finding. Negative symptoms of psychotic disorder include apathy and amotivation (Correll, & Schooler., 2020.). An improvement at six months may suggest the patient is experiencing less avoidance and is more engaged in life, hinting at an improved quality of life. The PANSS-Total score was near significance while the MANSA scale reporting on the subjective quality of life changed positively. A larger, longer, more detailed study might be able to establish if these positive trends are associated with treatment.

We believe these findings are consistent with previous research suggesting EMDR can benefit patients with a psychotic disorder who have experienced traumatic life events (Zhao et al., 2023). Research from the Netherlands has suggested that EMDR may reduce PTSD symptoms in patients with psychotic disorder (Van den Berg et al 2015, De Bont et al 2016). Analysis of larger datasets from the Netherlands describe a positive impact of EMDR therapy on paranoid symptoms of psychotic disorder and rates of remission for psychotic disorders (De Bont et al 2013).

Limitations

The strengths of this study include the real-world setting of the study in a routine NHS service and pragmatic delivery of the EMDR therapy.

Limitations include firstly the small sample size. We need to be modest in our claims of effectiveness, and both type 1 and type 2 errors are possible in exploratory trials. Anecdotally, no adverse events were noted but further research is required to assess the safety of providing EMDR in such settings.

Secondly the sample size was determined by ability to practically deliver in a naturalistic setting without dedicated funding. This study was set up as an exploratory trial and thus we hoped it would meaningfully inform further larger studies. Participation was by those who indicated an acknowledgement of the relevance of traumatic experiences with respect to their current difficulties thus needing a degree of insight into the relevance of traumatic experiences and intrigued by the offer of trauma-focused therapy. Whilst effort was made to ensure that all patients who were eligible were approached it was not possible to undertake systematic screening of eligible

caseloads. Potential recruits were identified by the research team through discussions and promotion of the study across local services. Some patients may therefore have been missed or not approached due to factors other than those detailed in the inclusion criteria. The study sample was also restricted to patients enthusiastic about receiving EMDR when approached. The length of time needed to recruit participants could indicate that there are a limited proportion of patients with psychotic disorder who consider their traumatic experiences need addressing. The randomization process was employed to negate any potential for cherry picking of patients perceived as likely benefactors of EMDR therapy. There is slight discrepancy of dropouts between groups, but not significantly so. Also, the difference is in opposite directions at the two timepoints, so there seems no common trend, which is reassuring.

Thirdly the team did not collect potentially confounding information such the prescribing of psychotropics and if their psychotropic treatment changed during the study period. The study did not capture other potentially confounding data such as educational status of participants, socioeconomic deprivation by postcode and the presence or absence of family or carer support. The clinical details of the traumatic events that participants disclosed were not captured nor was there a formal definition or assessment of adverse events. There was no active control intervention or formal assessment of treatment fidelity or tolerability.

Finally, research into economic modelling of the intervention, especially focused on quality of life, was not undertaken.

Despite these limitations, the pragmatic nature of the trial lends credence to the likelihood that this intervention may be beneficial in routine clinical settings when patients are open to receiving EMDR therapy.

Conclusion:

This was a pragmatic study exploring the impact of providing a short course of a standardized EMDR therapy for patients with a psychotic disorder seeking trauma-focused therapy in routine community psychiatric care. EMDR may reduce the impact of traumatic events in this patient group and the effect may persist for six months. This study adds to the growing evidence that EMDR may be an effective tool to help people with psychotic disorder who have experienced trauma in their lives. Further research is required to establish the cost-effectiveness of such treatment in this cohort and to build the evidence for any specific modifications to the standard protocol required for people with psychotic disorder to optimize effectiveness further.

Data availability statement: Data from the project used to provide this paper is available freely from - https://pearl.plymouth.ac.uk/handle/10026.1/18967

References

Adams, R., Ohlsen, S., & Wood, E. (2020). Eye Movement Desensitization and Reprocessing (EMDR) for the treatment of psychosis: a systematic review. *European journal of psychotraumatology*, *11*(1), 1711349. https://doi.org/10.1080/20008198.2019.1711349

Blanchard, E. B., Jones-Alexander, J., Buckley, T. C., & Forneris, C. A. (1996). Psychometric properties of the PTSD Checklist (PCL). *Behaviour research and therapy*, *34*(8), 669–673. https://doi.org/10.1016/0005-7967(96)00033-2

Brand, R. M., McEnery, C., Rossell, S., Bendall, S., & Thomas, N. (2018). Do trauma-focussed psychological interventions have an effect on psychotic symptoms? A systematic review and meta-analysis. *Schizophrenia research*, *195*, 13–22. https://doi.org/10.1016/j.schres.2017.08.037

Center for Substance Abuse Treatment (US). (2014). *Trauma-Informed Care in Behavioral Health Services*. Substance Abuse and Mental Health Services Administration (US).

Correll, C. U., & Schooler, N. R. (2020). Negative Symptoms in Schizophrenia: A Review and Clinical Guide for Recognition, Assessment, and Treatment. *Neuropsychiatric disease and treatment*, *16*, 519–534. https://doi.org/10.2147/NDT.S225643

Creamer, M., Bell, R., & Failla, S. (2003). Psychometric properties of the Impact of Event Scale - Revised. *Behaviour research and therapy*, *41*(12), 1489–1496. https://doi.org/10.1016/j.brat.2003.07.010

de Bont, P. A., van Minnen, A., & de Jongh, A. (2013). Treating PTSD in patients with psychosis: a within-group controlled feasibility study examining the efficacy and safety of evidence-based PE and EMDR protocols. *Behavior therapy*, *44*(4), 717–730. https://doi.org/10.1016/j.beth.2013.07.002

de Bont, P. A., van den Berg, D. P., van der Vleugel, B. M., de Roos, C., de Jongh, A., van der Gaag, M., & van Minnen, A. M. (2016). Prolonged exposure and EMDR for PTSD v. a PTSD waiting-list condition: effects on symptoms of psychosis, depression and social functioning in patients with chronic psychotic disorders. *Psychological medicine*, *46*(11), 2411–2421. https://doi.org/10.1017/S0033291716001094

de Bont, P., de Jongh, A., & van den Berg, D. (2019). Psychosis: An emerging field for EMDR research and therapy. *Journal of EMDR Practice and Research, 13*(4), 313–324. https://doi.org/10.1891/1933-3196.13.4.313

Fares-Otero, N., Alameda, L., Pfaltz, M., Martinez-Aran, A., Schäfer, I., & Vieta, E. (2023). Examining associations, moderators and mediators between childhood maltreatment, social functioning, and social cognition in psychotic disorders: A systematic review and meta-analysis. Psychological Medicine, 1-24. doi:10.1017/S0033291723001678

Kay, S. R., Fiszbein, A., & Opler, L. A. (1987). The positive and negative syndrome scale (PANSS) for schizophrenia. *Schizophrenia bulletin*, *13*(2), 261–276. https://doi.org/10.1093/schbul/13.2.261

Kay, S. R., Opler, L. A., & Lindenmayer, J. P. (1989). The Positive and Negative Syndrome Scale (PANSS): rationale and standardisation. *The British journal of psychiatry. Supplement*, (7), 59–67

Kim, D., Choi, J., Kim, H. S., Oh, D. H., Park, S. C., Lee, S. H. (2010). A pilot study of brief Eye Movement Desensitization and Reprocessing (EMDR) for treatment of acute phase schizophrenia. Korean Journal of Biological Psychiatry, 17(2), 94–102.

Laugharne, R., Marshall, D., Laugharne, J., & Hassard, A. (2014). A role for EMDR in the treatment of trauma in patients suffering from a psychosis: Four vignettes. *Journal of EMDR Practice and Research, 8*(1), 19–24. https://doi.org/10.1891/1933-3196.8.1.19

Matheson, S. L., Shepherd, A. M., Pinchbeck, R. M., Laurens, K. R., & Carr, V. J. (2013). Childhood adversity in schizophrenia: a systematic meta-analysis. *Psychological medicine*, *43*(2), 225–238. https://doi.org/10.1017/S0033291712000785

McGoldrick, T, Begum, M, Brown, KW (2008) EMDR and olfactory reference syndrome a case series. Journal of EMDR Practice and Research, 2: 63–8. DOI: 10.1891/1933-3196.2.1.63

National Collaborating Centre for Mental Health, (UK), 2014. Psychosis and schizophrenia in adults: treatment and management. The British Psychology Society and the Royal College of Psychiatrists. 2014; https://www.nice.org.uk/guidance/cg178/evidence/full-guideline-490503565 Retrieved on 12 January 2023

Priebe, S., Huxley, P., Knight, S., & Evans, S. (1999). Application and results of the Manchester Short Assessment of Quality of Life (MANSA). *The International journal of social psychiatry*, *45*(1), 7–12. https://doi.org/10.1177/002076409904500102

Sin, J., Spain, D., Furuta, M., Murrells, T., & Norman, I. (2017). Psychological interventions for post-traumatic stress disorder (PTSD) in people with severe mental illness. *The Cochrane database of systematic reviews*, *1*(1), CD011464. https://doi.org/10.1002/14651858.CD011464.pub2

The Centre for Addiction and Mental Health (CAMH) https://www.camh.ca/en/health-info/mental-illness-and-addiction-index/trauma#:~:text=Trauma%20is%20the%20lasting%20emotional,regulate%20emotions%20and%20navigate%20relationships. Retrieved on 4 November 2023

Valiente-Gómez, A., Moreno-Alcázar, A., Treen, D., Cedrón, C., Colom, F., Pérez, V., & Amann, B. L. (2017). EMDR beyond PTSD: A Systematic Literature Review. *Frontiers in psychology*, *8*, 1668. https://doi.org/10.3389/fpsyg.2017.01668

Van den Oord, E. J., Rujescu, D., Robles, J. R., Giegling, I., Birrell, C., Bukszár, J., Murrelle, L., Möller, H. J., Middleton, L., & Muglia, P. (2006). Factor structure and external validity of the PANSS revisited. *Schizophrenia research*, *82*(2-3), 213–223. https://doi.org/10.1016/j.schres.2005.09.002

van den Berg, D. P., & van der Gaag, M. (2012). Treating trauma in psychosis with EMDR: a pilot study. *Journal of behavior therapy and experimental psychiatry*, *43*(1), 664–671. https://doi.org/10.1016/j.jbtep.2011.09.011

Van den Berg, D.P., van der Vleugel, B.M., Staring, A.B., de Bont, P.A., de Jongh, A., (2013). EMDR in psychosis: Guidelines for conceptualization and treatment. Journal of EMDR Practice and Research 7, 208-224. DOI:10.1891/1933-3196.7.4.208

Van den Berg, D. P., de Bont, P. A., van der Vleugel, B. M., de Roos, C., de Jongh, A., Van Minnen, A., & van der Gaag, M. (2015). Prolonged exposure vs eye movement desensitization and reprocessing vs waiting list for posttraumatic stress disorder in patients with a psychotic disorder: a randomized clinical trial. *JAMA psychiatry*, *72*(3), 259–267. https://doi.org/10.1001/jamapsychiatry.2014.2637

Varese, F., Smeets, F., Drukker, M., Lieverse, R., Lataster, T., Viechtbauer, W., Read, J., van Os, J., & Bentall, R. P. (2012). Childhood adversities increase the risk of psychosis: a meta-analysis of patient-control, prospective- and cross-sectional cohort studies. *Schizophrenia bulletin*, *38*(4), 661–671. https://doi.org/10.1093/schbul/sbs050

Weiss, D. S., & Marmar, C. R. (1997). The Impact of Event Scale—Revised. In J. P. Wilson & T. M. Keane (Eds.), *Assessing psychological trauma and PTSD* (pp. 399–411). The Guilford Press.

WHO releases guidance on mental health care after trauma. (2013). *Central European journal of public health*, *21*(3), 127.

World Health Organization. (1993). The ICD-10 classification of mental and behavioural disorders: Diagnostic criteria for research. Geneva: World Health Organization.

Zhao, J., Chen, D. Y., Li, X. B., Xi, Y. J., Verma, S., Zhou, F. C., & Wang, C. Y. (2023). EMDR versus waiting list in individuals at clinical high risk for psychosis with post-traumatic stress symptoms: A randomized controlled trial. *Schizophrenia research*, *256*, 1–7. https://doi.org/10.1016/j.schres.2023.04.003

Table 1 - Demographic and baseline scores

		TAU (n=12)		EMDR (n=24)	
		n	Summary	n	Summary
Age		12	34.4 (SD11.3)	24	42.0 (SD 14.5)
Sex	Female	12	6 (50%)	24	14 (58%)
	Male		6 (50%)		10 (42%)
Diagnosis*	Bipolar	12	1 (8%)	24	6 (25%)
	PTSD		2 (17%)		6 (25%)
	Schizophrenia		9 (75%)		14 (58%)
	Schizoaffective disorder		1 (8%)		3 (13%)
Substance Use	Cannabis	12	1 (8%)	24	4 (17%)
	Cannabis and amphetamine		1 (8%)		0 (0%)
	Ketamine		1 (8%)		0 (0%)
	None		9 (75%)		20 (83%)
Impact of Events Scale – Revised (IES-R)	Total	11	53.0 (SD 14.6)	22	53.8 (SD 14.5)
	Avoidance subscale (IES-A)		18.2 (SD 6.8)	22	18.9 (SD 6.9)
	Intrusion subscale (IES-I)		18.8 (SD 7.9)	22	19.7 (SD 7.3)
	Hyperarousal subscale (IES-H)		16.0 (SD 5.1)	22	15.2 (SD 4.7)
Positive and Negative Symptoms of Schizophrenia scale (PANSS)	Total	11	67.0 (SD 18.9)	22	73.9 (SD 22.5)
	Positive symptoms subscale (PANSS-P)		15.6 (SD 6.3)	22	17.4 (SD 6.2)
	Negative symptoms subscale (PANSS-N)		14.4 (SD 6.7)	22	16.8 (SD 7.5)
	General psychopathology subscale (PANSS-G)		37.0 (SD 8.2)	22	39.7 (SD 11.3)

PTSD Checklist – Civilian (PCL-C)	11	57.2 (SD 13.9)	23	56.5 (SD 9.4)
Manchester Short Assessment of Quality of Life (MANSA)	11	50.5 (SD 9.7)	21	43.3 (SD 8.9)

Key:
Summary statistics: mean score ± standard deviation, or number (percentage)
(*) Patients can have more than one diagnosis. Percentage values many not add up to 100%.

Table 2 – Outcomes at completion of treatment (10 weeks from baseline)

Table 2 – Outcomes at completion of treatment (10 weeks from baseline)								
Outcome		Group	n	Baseline mean±SD	10 weeks mean±SD	Group Difference* mean (95% CI)	P-value	Effect size+
Impact of Events Scale – Revised (IES-R)	Total Score (IES-Total)	TAU	8	49.9(SD 14.0)	52.9(SD 12.8)	-21.3 (-40.6,-2.0)	**0.03**	1.49
		EMDR	18	53.6(SD 13.6)	34.4(SD 26.9)			
	Avoidance subscale (IES-A)	TAU	8	17.0(SD 7.2)	16.3(SD 8.8)	-5.3 (-12.8, 2.1)	0.15	0.79
		EMDR	18	19.4(SD 5.1)	12.2(SD 8.8)			
	Intrusion subscale (IES-I)	TAU	8	17.8(SD 8.9)	20.4(SD 6.8)	-9.6 (-18.3, -1.0)	**0.03**	-1.31
		EMDR	18	19.3(SD 7.5)	11.7(SD 10.8)			
	Hyper arousal subscale (IES-H)	TAU	8	15.1(SD 4.7)	16.2(SD 3.6)	-5.7 (-12.1,0.6)	0.06	-1.20
		EMDR	18	15.0(SD 5.0)	10.4(SD 8.8)			
Positive and Negative Symptoms of Schizophrenia scale (PANSS)	Total Score (PANSS-Total)	TAU	8	68.0(SD 18.0)	65.3(SD 17.2)	-4.9 (-20.1, 0.4)	0.52	0.23
		EMDR	18	69.7(SD 22.5)	61.3(SD 22.3)			
	Positive symptoms subscale (PANSS-P)	TAU	8	14.9(SD 5.4)	13.4(SD 5.2)	-0.2 (-4.6, 4.2)	0.92	0.03
		EMDR	18	16.8(SD 6.1)	14.5(SD 6.9)			
	Negative symptom subscale (PANSS-N)	TAU	8	14.8(SD 7.0)	16.3(SD 7.4)	-2.5 (-6.8, 1.7)	0.23	0.35
		EMDR	18	14.9(SD 6.5)	13.8(SD 5.7)			
		TAU	8	38.4(SD 7.9)	35.6(SD 9.5)	-2.4 (-10.8, 6.0)	0.56	0.23

	General psychopathology subscale (PANSS-G)	EMDR	18	37.9(SD 11.5)	33.0(SD 11.5)			
PTSD Checklist – Civillian (PCL-C)		TAU	8	55.0(SD 13.3)	56.9(SD 11.5)	-14.7 (-27.4, -2.2)	**0.02**	1.36
		EMDR	19	56.8(SD 9.9)	42.9(SD 16.1)			
Manchester Short Assessment of Quality of Life (MANSA)		TAU	8	52.1(SD 8.3)	49.6(SD 11.0)	4.9 (-4.5, 14.3)	0.29	0.51
		EMDR	19	43.9(SD 9.4)	48.7(SD 11.7)			

Key:

(*) Group difference at 10 weeks, adjusted for scores at baseline
(+) Effect size is Cohen's d

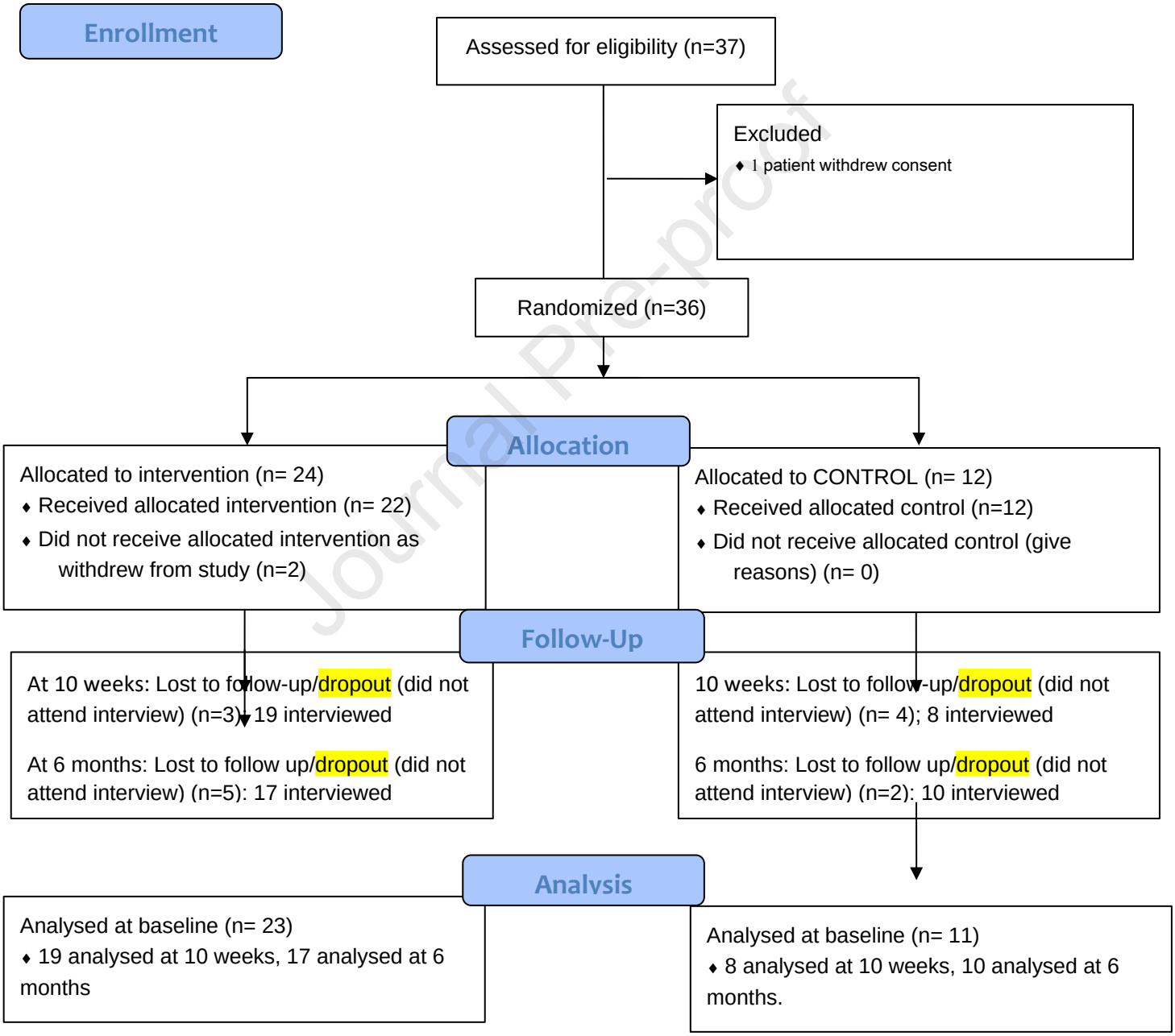
Table 3 – Outcomes at 6-month follow-up

Outcome		Group	n	Baseline Mean (SD)	6 months Mean(SD)	Group Difference* mean (95% CI)	P-value	Effect size+
Impact of Events Scale – Revised (IES-R)	Total Score (IES-Total)	TAU	10	50.8(SD 13.3)	52.0(SD 12.2)	-17.5 (-34.4, -0.6)	**0.04**	1.22
		EMDR	16	55.3(SD 14.1)	37.1(SD 25.1)			
	Avoidance subscale (IES-A)	TAU	10	17.5(SD 6.8)	17.1(SD 6.4)	-3.6 (-10.2, 3.0)	0.27	0.54
		EMDR	16	18.5(SD 5.3)	14.0(SD 9.1)			
	Intrusion subscale (IES-I)	TAU	10	18.1(SD 7.9)	21.0(SD 7.2)	-6.5 (-13.4, 0.5)	0.07	0.88
		EMDR	16	19.3(SD 5.6)	13.2(SD 9.6)			
	Hyper arousal subscale (IES-H)	TAU	10	15.1(SD 4.6)	15.6(SD 3.6)	-5.8 (-11.1, -0.5)	**0.03**	1.21
		EMDR	16	15.8(SD 4.8)	10.1(SD 7.8)			
Positive and Negative Symptoms of Schizophrenia scale (PANSS)	Total Score (PANSS-Total)	TAU	10	68.2(SD 19.5)	67.9(SD 22.7)	-14.2 (-30.6, 2.2)	0.09	0.67
		EMDR	16	73.4(SD 23.7)	56.6(SD 22.9)			
	Positive symptoms subscale (PANSS-P)	TAU	10	15.7(SD 6.6)	15.2(SD 6.3)	-2.7 (-6.9, 1.6)	0.20	0.43
		EMDR	16	17.8(SD 6.2)	13.8(SD 6.4)			
	Negative symptom subscale (PANSS-N)	TAU	10	14.6(SD 7.0)	16.0(SD 6.7)	-4.1 (-7.8, -0.4)	**0.03**	0.57
		EMDR	16	15.5(SD 7.0)	12.3(SD 4.4)			
	General psychopathology subscale (PANSS-G)	TAU	10	37.9(SD 8.0)	36.7(SD 11.0)	-7.4 (-16.8, 1.9)	0.11	0.72
		EMDR	16	40.1(SD 11.9)	30.5(SD 13.1)			
PTSD Checklist – Civilian (PCL-C)		TAU	10	54.7(SD 11.8)	54.1(SD 12.9)	-12.6 (-25.9, 0.8)	0.06	1.15

	EMDR	16	57.8(SD 10.0)	43.4(SD 18.8)			
Manchester Short Assessment of Quality of Life (MANSA)	TAU	10	52.5(SD 7.6)	52.6(SD 9.1)	-0.9 (-10.7, 8.9)	0.85	0.09
	EMDR	15	43.1(SD 9.3)	50.5(SD 10.4)			
Key: (*)Group difference at 6 months, calculated as value for EMDR group minus value for TAU group. Adjusted for scores at baseline (+) Effect size is Cohen's d							

CONSORT
TRANSPARENT REPORTING of TRIALS

CONSORT 2010 Flow Diagram



Highlights

1. This study is a randomized exploratory trial of prospective treatment of EMDR and six-month follow-up for people with psychotic disorder with an interim 10-week analysis.

2. This is the first study demonstrating effectiveness of EMDR for people with psychotic disorder and trauma in British routine psychiatric settings.

3. This study is important as people with psychotic disorder are often excluded from EMDR trials, while our evidence suggests that may benefit from EMDR therapeutically.

All authors satisfy the ICMJE guidance by substantially contributing to the design, analysis and interpretation of the work, drafting of the manuscript, final approval of the manuscript and all agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work is appropriately investigated and resolved.

A pragmatic randomised controlled exploratory trial of the effectiveness of EMDR therapy for psychosis

No known conflict of interest exists for any of the authors involved in this manuscript.