Digitally supported CBT to reduce paranoia and improve reasoning for people with schizophrenia-spectrum psychosis: the SlowMo RCT

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Scientific summary

The SlowMo RCT

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Scientific summary

Background

Paranoia, or the fear of deliberate harm from others, is one of the most common symptoms of schizophrenia-spectrum disorders and is associated with significant distress and disruption to the person's life. Developing effective interventions for paranoia is, therefore, a clinical priority. The National Institute for Health and Care Excellence recommends cognitive–behavioural therapy for psychosis, including paranoia. Meta-analytical studies of first-generation cognitive–behavioural therapy for psychosis have found small to medium sized beneficial effects on delusions, including paranoia, or positive symptoms more broadly. However, there remain significant challenges to access, engagement, adherence and effectiveness of cognitive–behavioural therapy.

We have approached this challenge in two main ways: first, by adopting an interventionist causal approach to increase cognitive–behavioural therapy for psychosis effectiveness, and, second, by incorporating inclusive human-centred design methods to enhance the user experience of therapy and improve engagement and adherence. The interventionist causal approach to improving therapy effectiveness involves identifying mechanisms that play a causal role in paranoia (e.g. reasoning) and then developing tailored interventions. SlowMo focuses on fast reasoning processes that are robustly associated with paranoia: the jumping to conclusions bias (forming rapid judgements focused on a small amount of information) and the belief inflexibility bias (defined as the metacognitive capacity of reflecting on one's beliefs, changing them in the light of reflection and evidence, and generating and considering alternatives). We have developed a new cognitive–behavioural intervention, SlowMo, that aims to enhance the impact on paranoia and reasoning by helping people to be aware of their tendency to jump to conclusions, and then intensively targeting belief flexibility to promote slow thinking. The inclusive, human-centred design of SlowMo was intended to promote its ease of use, appeal and perceived usefulness, and to address the needs of those for whom the content and process of standard therapy presents barriers to engagement and adherence. The SlowMo intervention represents the end point of a decade of development and, to the best of our knowledge, is the first blended digital psychological therapy for paranoia. It consists of face-to-face therapy sessions supported by digital technology and a personalised mobile telephone application (hereafter referred to as 'mobile app') for use in daily life.

Objectives

The research questions were:

1. Is SlowMo efficacious in reducing paranoia severity over 24 weeks when added to treatment as usual, compared with treatment as usual alone?
2. Does SlowMo lead to changes in the following outcomes: reasoning, well-being, quality of life, self-schemas and others schemas, service use and worry?
3. Does SlowMo reduce paranoia severity by improving fast thinking (reducing belief inflexibility and jumping to conclusions)?
4. Do participants' characteristics (i.e. their cognitive capacities, specifically working memory and thinking habits; and their symptoms, specifically negative symptoms) moderate the effects of the intervention?
5. Does outcome differ by adherence to the intervention?
6. Is SlowMo therapy, including the digital platform, acceptable, as assessed by therapy uptake and session adherence?
7. The service user experience of the therapy and its impact on outcomes are further explored in relation to pre-therapy digital literacy, mobile app adherence and technical problems, and a co-produced qualitative interview study with service user researchers.

Primary hypotheses

1. The intervention will reduce paranoia severity over 24 weeks.
2. Fast thinking (belief inflexibility and jumping to conclusions) will improve in response to the intervention.
3. Reductions in fast thinking will mediate positive change in paranoia severity.

Secondary hypotheses

4. Poorer working memory and more severe negative symptoms will negatively moderate treatment effects.
5. Therapy adherence will moderate the effects of treatment on outcome.
6. Worry will not mediate reductions in paranoia severity.

Methods

We conducted a parallel-arm, assessor-blind, randomised controlled trial with 1 : 1 allocation to test the efficacy of the SlowMo intervention in reducing paranoia severity when added to treatment as usual, compared with treatment as usual alone. Participants were recruited from NHS mental health services with the same procedures across three main trial sites and from three additional patient identification centres.

The trial received a favourable ethics opinion from Camberwell St. Giles Research Ethics Committee (reference 16/LO/1862; Integrated Research Administration System 206680). The trial protocol, including all study hypotheses, was published.

The participant inclusion criteria were participants aged ≥ 18 years; with persistent (≥ 3 months) distressing paranoia; with a diagnosis of schizophrenia-spectrum psychosis; with the capacity to provide informed consent; and with a sufficient grasp of English to participate in trial processes. The participant exclusion criteria were profound visual and/or hearing impairment; the inability to engage in the assessment procedure; being currently in receipt of other psychological therapy for paranoia; and a primary diagnosis of substance abuse disorder, personality disorder, organic syndrome or learning disability. All participants gave written informed consent.

An online, independent system randomised eligible participants (1 : 1) using randomly varying permuted blocks, stratified by site and baseline paranoia severity, to the SlowMo intervention with treatment as usual (SlowMo group), or to treatment as usual alone (control group). Research assessors, who were graduate psychologists, were masked to therapy allocation.

SlowMo therapy consisted of eight individual face-to-face sessions, with each module addressing a specific topic and typically lasting 60–90 minutes. The therapy was delivered by trained therapists within a 12-week time frame and was assisted by a web-based application (hereafter referred to as web app), delivered using a touchscreen laptop (the 'SlowMo web app'), with interactive features, including information, vignettes, games and personalised content, which was synchronised with a native mobile app installed on a standard Android (Google Inc., Mountain View, CA, USA) smartphone provided to participants, to assist therapy generalisation.

The uptake of therapy delivery was assessed by the number and duration of sessions attended, and the adherence to the treatment manual, using a therapy checklist, was defined as no more than one web app component missed for any attended therapy session. Adherence to the mobile app was operationalised as at least one out-of-session interaction for a minimum of three of the therapy sessions, measured by system analytics. Self-reported user experience and adherence to the mobile app were also assessed.

The user experience was further explored in a co-produced study of 22 qualitative interviews led by service user researchers.

Treatment as usual was delivered in accordance with national and local service protocols and guidelines. This usually consists of prescription antipsychotic drugs, contact with a community mental health worker and regular outpatient appointments with a psychiatrist. Participation did not alter usual treatment decisions about medication or additional psychosocial interventions that were recorded in both groups.

Assessments of outcomes were completed at 0 weeks (baseline), 12 weeks (end of therapy) and 24 weeks (follow-up). Blinded research assessors conducted the enrolment and assessments.

Outcomes

The primary outcome measure was paranoia measured by the Green Paranoid Thoughts Scale, measured with the Revised-Green Paranoid Thoughts Scale, and observer-rated measures of persecutory delusions (Psychotic Symptom Rating Scales delusion scale and delusions items of the Scale for the Assessment of Positive Symptoms). Other outcome measures were reasoning measures, using measures of belief flexibility (measured as possibility of being mistaken and alternative explanations), jumping to conclusions and fast and slow thinking scales; and published measures of well-being, quality of life, self-schemas and other schemas, service use and worry. Clinical and cognitive characteristics, assessed at baseline only, were examined as potential moderators of treatment effects. Adverse events were actively monitored for the duration of the study up to the 24-week follow-up.

Statistical analysis

We powered the study to detect a clinically meaningful 10-point reduction in the Green Paranoid Thoughts Scale total score (effect size 0.4) and accounted for the partial nested design owing to clustering in the SlowMo group. With the 1 : 1 allocation and 0.05 significance level, a simple two-tailed *t*-test with 150 people per group had 90% power to detect an effect size of 0.4 and 80% power to detect an effect size of 0.35. To allow for 20% attrition, we aimed to recruit 360 participants at baseline, split equally across the three sites (120 per site, 60 per group per site). All analyses were performed using the intention-to-treat population and incorporated data from all participants, including those who did not complete therapy. The statistical analysis plan was agreed with an independent Data Monitoring and Ethics Committee before any inspection of post-randomisation data by the research team.

To test the primary hypothesis that the intervention would reduce paranoia severity over 24 weeks, we fitted a linear mixed model, allowing for clustering by both participants and therapists, to the repeated measures of GPTS, with fixed effects of randomised group, time, time by randomised group interaction, treatment site, baseline paranoia severity and baseline Green Paranoid Thoughts Scale. The treatment effect (adjusted between-group mean difference) was estimated from the model for each time point separately. All secondary outcome measures were analysed using the same modelling approach, using linear mixed models for continuous outcomes and logistic mixed models for binary outcomes. Cohen's *d* effect sizes at 12 and 24 weeks were calculated as the adjusted mean difference of the outcome divided by the sample standard deviation of the outcome at baseline. Causal mediation analysis was performed using parametric regression models and moderation analyses were conducted by adding interaction terms between randomised group and a set of prespecified moderators.

Results

From 1 May 2017 to 14 May 2019, we assessed 604 people for eligibility and, of these, recruited 362 participants: 181 were randomly allocated to the SlowMo intervention group and 181 to the control group. There was one post-randomisation withdrawal. The final sample was, therefore,

361 participants. Data were available for over 90% of the sample at each follow-up point (12 weeks: $n = 328$, 91%; 24 weeks: $n = 333$, 92%). A total of 145 (80%) of those randomised to the SlowMo group ($n = 181$) completed all eight therapy sessions. Adherence to the delivery of the web app content was high, with adherence ratings of $\geq 90\%$ for each of the eight sessions. Excellent rates of self-reported and system analytics mobile app adherence were found, with the criteria for mobile app adherence met by 71.4% of eligible participants. Most people reported that the mobile app was easy to use, enjoyable and useful. Positive experiences of SlowMo as a blended intervention were reported in the qualitative interviews.

SlowMo was superior to usual care in reducing paranoia on all three measures used: Green Paranoid Thoughts Scale total at 12 weeks (Cohen's $d = 0.30$, 95% confidence interval 0.09 to 0.51; $p = 0.005$) and 24 weeks (Cohen's $d = 0.20$, 95% confidence interval–0.02 to 0.40; $p = 0.063$); Psychotic Symptom Rating Scales delusions at 12 weeks (Cohen's $d = 0.47$, 95% confidence interval 0.17 to 0.78; $p = 0.002$) and 24 weeks (Cohen's $d = 0.50$, 95% confidence interval 0.20 to 0.80; $p = 0.001$); and Scale for the Assessment of Positive Symptoms persecutory delusions at 12 weeks (Cohen's $d = 0.43$, 95% confidence interval 0.03 to 0.84; $p = 0.035$) and 24 weeks (Cohen's $d = 0.54$, 95% confidence interval 0.14 to 0.94; $p = 0.009$).

Treatment effects were found for some, but not all, of the reasoning measures. For the measures of belief flexibility and possibility of being mistaken, both percentage uncertainty and dichotomous rating improved significantly, but these did not improve for alternative explanations. Jumping to conclusions showed little evidence of improvement (only one significant finding, number of beads drawn at 12 weeks, out of a total of eight task scores). The fast scale of the Fast and Slow Thinking Questionnaire showed improvements at both time points. Improvements, with a small effect size of approximately Cohen's $d = 0.3$, were found for SlowMo in nearly all other secondary outcome measures – well-being, quality of life, worry and self-concept – at either or both time points, most consistently at the 24-week follow-up. Baseline characteristics did not moderate treatment effects. Changes in belief flexibility and worry mediated changes in paranoia. A total of 54 adverse events were reported, 51 serious events occurring in 19 people in the SlowMo group and 21 serious events in the control group, and no deaths.

Conclusions

To the best of our knowledge, SlowMo is the largest trial to date, undertaken in a clinical population, of psychological therapy for fear of harm from others (paranoia). The recruitment target of 362 participants was met, with over 90% of participants followed up at each time point. We addressed two goals: to improve effectiveness, and to overcome barriers to engagement and adherence. These results suggest that SlowMo is clinically effective and has an excellent user experience, thereby supporting adherence. We found consistent, significant effects of SlowMo when added to treatment as usual compared with treatment as usual alone, over and above the generally improving trajectory of both groups. Improvements were demonstrated for all of the paranoia and persecutory delusions outcomes across the 6 months (ranging from small to medium effect sizes), as well as improvements in aspects of belief flexibility and reasoning, and in well-being, quality of life, self-concept and worry.

Therapy uptake, adherence and self-reported user experience were all in the upper range, and pre-therapy demographic differences in smartphone use and confidence did not have an impact on mobile app adherence, suggesting that SlowMo is highly acceptable, easy to use and enjoyable for a diverse user population. Peer researcher-led qualitative interviews highlighted the central role of the supportive therapists and that the digital component of the therapy augmented the rich therapeutic relationship.

The intervention effects were not moderated by our baseline measures and hypothesised characteristics, indicating that the intervention is equally beneficial regardless of cognitive capacity or baseline symptoms. The treatment targeted reasoning to improve paranoia; we found that outcome was mediated by

improvement in a key aspect of reasoning, belief flexibility (possibility of being mistaken) and, unexpectedly, by changing worry. We had hypothesised that the primary process underpinning change would be through reasoning; however, these findings suggest the potential for other processes to be involved in treatment effects, consistent with a multifactorial theory of change. We found no evidence of the intervention being harmful. Both groups generally improved across the course of the trial and there were similar numbers of serious adverse events across the two conditions. Limitations include the treatment as usual comparator; therefore, the design could not control for any effects of time with a therapist. The qualitative interviews and user experience survey also identified some technical challenges and desirable improvements in the digital technology; this is information that we will use to support the next iteration of the SlowMo blended therapy.

The SlowMo trial has demonstrated clinically worthwhile results, with consistent, sustained positive effects across a range of outcomes. These effects match or exceed those typically observed for standard cognitive–behavioural therapy for psychosis, but were achieved in fewer sessions, and were accompanied by excellent engagement and retention, validating the therapy redesign.

Recommendations for future research

1. The trial results argue for further implementation studies testing SlowMo's real-world delivery within clinical pathways for persecutory delusions in a range of clinical settings.
2. The results indicate that the treatment worked, in part, through helping people to slow down their thinking and to worry less. Further research examining the mechanisms that mediate these treatment effects is recommended.
3. Our findings underscore the value of focusing on both effectiveness and user experience when developing digital therapeutics, and we strongly advocate adoption of this strategy to improve outcomes for people with psychosis.

Trial registration

The trial is registered as ISRCTN32448671.

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