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Long-Term Effectiveness of Cognitive Therapy for Refractory Social Anxiety Disorder: One-Year Follow-Up of a Randomized Controlled Trial

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Dear Editor,

There is a large body of evidence that antidepressants and cognitive therapy (CT) are beneficial for the treatment of social anxiety disorder (SAD) [1]. Although individual CT has recently been regarded as the first-choice treatment for SAD, antidepressants are still commonly used in clinical practice [2, 3]. Therefore, more work is required to garner evidence of next-step treatment options for SADs who have been ineffectively treated with antidepressants.

Only four studies have assessed augmentation or switching strategies for SADs who were refractory to antidepressants [4–7]. Among these next-step strategies, individual CT as an adjunct to usual care has achieved the highest rates of treatment response (85.7%) and remission (47.6%) at the end of treatment [4]. Conversely, other medication augmentation/switching strategies had response rates of 48.3–70.0% and remission rates of 18.6–27.0% [5–7]. However, these studies have only assessed short-term treatment outcomes (the longest being 24 weeks).

In this paper, we report on 1-year follow-up data evaluating the long-term effectiveness of individual CT in addition to usual care for antidepressant-refractory SAD in our previous randomized controlled trial [4], focusing on the adjunctive CT group. We supplementarily evaluated the cost-effectiveness of adjunctive CT, but the details are presented only in the online supplementary material (online suppl. Appendix; for all online suppl. material, see www.karger.com/doi/10.1159/000500108).

Eligible antidepressant-refractory SADs ($n = 42$) were randomly allocated to two groups to either receive individual CT in addition to usual care (adjunctive CT, $n = 21$) or usual care alone (UC alone, $n = 21$). Local primary psychiatrists referred patients to the trial but continued to provide usual care to patients in both groups. Seven therapists (4 clinical psychologists, 1 psychiatrist, 1 registered nurse, and 1 psychiatric social worker) delivered 16 individual weekly CT sessions based on the Clark and Wells model. Both groups received active interventions for 16 weeks, but thereafter, participants in the UC alone group were offered individual CT if desired (62% subsequently received individual CT; that data is not reported here).

The primary outcome was the severity level of social anxiety, using the Liebowitz Social Anxiety Scale-Self Report (LSAS-SR). Secondary self-reported outcome measures: Patient Health Questionnaire-9 item (PHQ-9), Generalized Anxiety Disorder-7 item (GAD-7), and EuroQol-5 Dimensions (EQ-5D). Data was collected for both groups at week 0 (pre-intervention: Pre), week 8 (mid-intervention: Mid), and week 16 (post-intervention: Post). For the adjunctive CT group, data was collected at week 20 (1-month follow-up: 1M-FU), week 28 (3-month follow-up: 3M-FU), week 40 (6-month follow-up: 6M-FU), and week 64 (1-year follow-up: 1Y-FU).

All analyses were performed using JMP 12 PRO (SAS Institute), and a two-tailed alpha level of 0.05 was used to define statistical significance. To assess long-term effectiveness of adjunctive CT, mean total scores at each assessment point for all outcomes were analyzed with single-factor (time) repeated measures analysis of variance (ANOVA). Where repeated measures ANOVA indicated significant changes, pairwise t tests were calculated post hoc. Primary analyses were based on the intent-to-treat principle without imputing missing data. For sensitivity analysis, the linear mixed model was also applied to examine effects of missing data.

There were no significant group differences in baseline clinical characteristics (see original trial [4]). Concerning attrition, one patient in the UC alone group dropped out during the short-term intervention period due to a worsening of depressive symptoms, and three patients in the adjunctive CT group dropped out during the follow-up period (1 moved, 1 unwilling to continue, and 1 work-related schedule conflict).

As shown in Figure 1, all primary and secondary outcomes in the adjunctive CT group were significantly improved by week 16 (Post), and observed improvements were maintained until the end of the follow-up (1M-FU). Two of the four measures (LSAS-SR and PHQ-9) showed significant improvements from Pre to Post and from Post to 1Y-FU. On the primary outcome (LSAS-SR), the Pre to Post and Pre to 1Y-FU within-group effect sizes of adjunctive CT were $d = 1.91$ and $d = 2.66$, respectively. At the 1Y-FU assessment, 85.7% of patients in the adjunctive CT group were judged to be responsive to the treatment (18/21, three dropped out), and 57.1% met the remission criteria (12/21). When carrying

Fig. 1. Observed long-term outcome data in the adjunctive CT group. [†] $p < 0.05$, significant difference in pairwise comparisons with week 0. [‡] $p < 0.05$, significant difference in pairwise comparisons with both weeks 0 and 16. Higher scores on the EQ-5D indicate better quality of life. Higher scores on the other measures indicate greater pathology or severity.

the last observation forward for dropouts, these percentages were 95.2% (responded) and 57.1% (remitted). See online supplementary Results for more details.

The findings of this study indicate that the effects of adjunctive CT seemed to be well maintained 1 year after completion of treatment for measures of social anxiety, depression, generalized anxiety, and quality of life. The Pre to 1Y-FU treatment effect size of adjunctive CT was large ($d = 2.66$). The course of improvement demonstrates that antidepressant-refractory SADs exhibit substantial treatment gains immediately following treatment and that these are well maintained at the 1-month, 3-month, 6-month, and 1-year follow-up points. These results are consistent with the favorable long-term effects of individual CT for SADs observed in previous studies also carried out over at least 1 year, which did not target antidepressant-refractory patients [e.g., 8–10]. Thus, the findings of our study underscore the long-term benefits of adjunctive CT in improving social anxiety and other related symptoms, even in antidepressant-refractory cases.

The main limitations of the study are: (a) small sample size, (b) lack of follow-up clinical outcome data in the UC alone group, and (c) lack of follow-up information regarding concurrent medication in both groups. We also could not determine whether adjunctive CT itself, or other non-treatment-specific factors, contributed to greater clinical effectiveness. The current study intended to examine the additional value of CT to usual care but was not an examination of the effectiveness of CT itself. To evaluate outcomes

with more confidence, a replication study is needed which employs a larger sample and obtains complete follow-up data including concurrent medication information. It would also be of interest to directly compare individual CT with other intervention-delivery methods (e.g., group based, internet based), with other forms of psychotherapy, and/or with other medications.

In conclusion, the results of this study suggest that adding CT to usual care for antidepressant-refractory SAD can produce substantial, maintained effects.

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Statement of Ethics

The study protocol has been reviewed and approved by the ethics committee at the Chiba University Graduate School of Medicine (reference number: 1422) and carried out in accordance with the World Medical Association Declaration of Helsinki. Written informed consent was obtained from all patients after the procedures had been fully explained.

Disclosure Statement

N.Y. has received writing honoraria from Igaku-Shoin, Medical Friends, Nihon-Hyounsha, and Sogensha. R.T. has received a speaking honorarium from Mitsubishi Tanabe Pharma and writing honorarium from Chugaiigakusha. The other authors declare no competing interests.

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Author Contributions

N.Y., K.Y., M.I., T.F., and E.S. conceptualized and designed this study. M.I. and E.S. coordinated the trial. N.Y. and R.T. collected data. E.S. administered supervised therapies and performed patients' screening. N.Y., K.K., K.Y., and T.F. substantially contributed to the data analysis, and all authors to the interpretation of the results. N.Y. and K.K. drafted the first manuscript, and all authors critically revised the first version for important intellectual content. All authors read and approved the final manuscript.

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