Metacognition in anxious-depression is state-dependent: an observational treatment study

Celine A Fox, M.S.[1,2,*], Chi Tak Lee, M.S.[1,2], Anna K Hanlon, M.S.[1,2], Tricia XF Seow, Ph.D.[3], Kevin Lynch, M.S.[1], Siobhán Harty, Ph.D.[4], Derek Richards, Ph.D.[1,4], Jorge Palacios, M.D., Ph.D.[1,4], Veronica O'Keane, M.D., Ph.D.[5,6], Klaas E Stephan, M.D., Ph.D.[7,8], Claire M Gillan, Ph.D.[1,2,9]

[1] Department of Psychology, Trinity College Dublin, Dublin, Ireland
[2] Trinity College Institute of Neuroscience, Trinity College Dublin, Dublin, Ireland
[3] Wellcome Centre for Human Neuroimaging, University College London, London, United Kingdom
[4] SilverCloud Science, SilverCloud Health Ltd, Dublin, Ireland
[5] Department of Psychiatry, Trinity College Dublin, Dublin, Ireland
[6] Tallaght Hospital, Trinity Centre for Health Sciences, Tallaght University Hospital, Tallaght, Dublin, Ireland
[7]Translational Neuromodeling Unit (TNU), Institute for Biomedical Engineering, University of Zurich & ETH Zurich, Zurich, Switzerland
[8] Max Planck Institute for Metabolism Research, Cologne, Germany
[9] Global Brain Health Institute, Trinity College Dublin, Dublin, Ireland

* Corresponding author. E-mail address: foxce@tcd.ie

DISCLOSURES

The PhD studentship of Ms. Lee is co-funded by SilverCloud Health and the Irish Research Council. Dr. Harty, Dr. Richards and Dr. Palacios are current employees of SilverCloud Health. Dr. Stephan acknowledges support by the René and Susanne Braginsky Foundation and the ETH Foundation. Ms. Fox, Ms. Hanlon, Dr. Seow, Mr. Lynch, Dr. O'Keane and Dr. Gillan report no financial relationships with commercial interests.

ACKNOWLEDGMENTS

This work was funded by a fellowship awarded to Dr. Gillan from MQ: transforming mental health (MQ16IP13). Dr. Gillan holds additional funding from Science Foundation Ireland's Frontiers for the Future Scheme (19/FFP/6418), and a European Research Council (ERC) Starting Grant (ERC-H2020-HABIT). The PhD studentship of Ms. Fox is funded by the Government of Ireland Postgraduate Scholarship Programme (GOIPG/2020/662). The authors thank all the participants for their involvement in this study. We thank the AWARE charity and the Berkshire foundation trust that supported recruitment for the iCBT arm. We thank the individual pharmacies and General Practitioner services for their support in recruiting the antidepressant arm.

ABSTRACT

Objective: Prior studies have found metacognitive impairments are linked to a transdiagnostic dimension of anxious-depression, manifesting as reduced confidence in performance ('metacognitive bias'). However, previous work has been cross-sectional and so it is unclear if under-confidence is a trait-like marker of anxious-depression vulnerability, or if it resolves when anxious-depression improves.
Methods: Data were collected as part of the 'Precision in Psychiatry' study, a large-scale transdiagnostic, four-week observational study of individuals initiating internet-based cognitive behavioural therapy (iCBT) or antidepressant medication. Self-reported clinical questionnaires and perceptual task performance were gathered to assess anxious-depression and metacognitive bias at baseline and four-week follow-up. Primary analyses were conducted for individuals who received iCBT (n=649), with comparisons between smaller samples that received antidepressant medication (n=88) and a control group receiving no intervention (n=82).
Results: Prior to receiving treatment, anxious-depression severity was associated with under-confidence in performance in the iCBT arm, replicating previous work. From baseline to follow-up, levels of anxious-depression were significantly reduced, and this was accompanied by a significant increase in metacognitive confidence (β=0.17, SE=0.02, p<0.001). These changes were correlated (r(647)=-0.12, p=0.002); those with the greatest reductions in anxious-depression levels had the largest increase in confidence. In the antidepressant arm, anxious-depression reduced (β=-0.61, SE=0.09, p<0.001) and confidence increased (β=0.31, SE=0.08, p<0.001). Among controls, confidence remained stable from baseline to follow-up (β=0.11, SE=0.07, p=0.103).
Conclusions: Metacognitive biases in anxious-depression are state-dependent; when symptoms improve with treatment, so does confidence in performance. Our results suggest this is not specific to the type of intervention.

INTRODUCTION

Metacognition refers to the ability to accurately monitor and appraise one's own cognitive experience (1). Metacognition is crucial for adaptive behaviour: it allows for flexible adjustment of behavioural strategies in order to improve performance, signals when to engage or withdraw from an activity, and guides the engagement in social interactions (2,3). Metacognitive abilities vary across individuals; one can be under- or over-confident, and these biases can be associated with maladaptive thoughts, feelings and behaviours (4). There is a growing interest in these confidence abnormalities in psychiatry, with studies implicating alterations of metacognition in depression, obsessive-compulsive disorder, and psychosis (5). While case-control studies have mainly found patterns of reduced confidence across several disorders, newer methods that can separate transdiagnostic dimensions of mental health using large online samples have revealed specific and bi-directional effects of confidence (6). Using these methods, studies have shown that the transdiagnostic dimension 'anxious-depression' is linked to under-confidence in one's own performance, while a separate dimension 'compulsivity and intrusive thought' is related to elevated confidence (7–11).

A major gap in this area is that studies to-date only measure metacognition and transdiagnostic psychopathology at a single time point. Therefore, it is unclear if metacognitive biases are stable, fixed traits, or if they might change with treatment response. Preliminary evidence suggests metacognition may indeed be malleable; metacognitive abilities can be improved with metacognitive interventions, such as training, in unselected online samples (12,13) and in clinical populations (14,15). However, it remains unknown if metacognitive changes generalise beyond its specific training context and are associated with any real-world improvement in psychiatric symptoms. In clinical studies, research has identified confidence abnormalities in at-risk populations (16,17), suggestive of a trait-dependence. In contrast, stimulant use disorders remitters have better metacognition than active users, suggesting state-dependence (18). Within-subject designs are needed to extend this work and understand if metacognition can improve in parallel to symptom alleviation, or if those with greater metacognitive deficits are simply the most vulnerable to illness onset and persistence.

The present study aimed to address this by examining metacognition in a large cohort of individuals before and after internet-based cognitive behavioural therapy (iCBT). iCBT has emerged as an important intervention for reducing the treatment-gap in mental healthcare provision globally; it is low-cost, scalable, geographically unconstrained and flexible (19,20). iCBT offers patients standardised content and records objective metrics of treatment engagement, making it particularly well-suited to treatment-oriented research in psychiatry (21). However, most studies on iCBT have examined clinical effectiveness (22–24), but little research on how it might impact on metacognition (25). In this study, we used an objective task measure of metacognition (26), which allowed us to test if successful treatment is linked to within-person improvements in metacognition. We also tested if any changes in metacognition were iCBT-specific, by comparing data gathered from smaller samples of individuals receiving antidepressant medication and a control group receiving no intervention. Similar to iCBT, antidepressants have established transdiagnostic efficacy (27–29), but studies typically lacked power to detect effects

of antidepressants on cognitive abilities (30–33). Accordingly, a secondary aim of this study was to compare metacognitive changes across the different intervention arms, which may shed light on differential therapeutic mechanisms and potentially augment therapeutic decision-making in the future.

METHODS

Participants

Participants were recruited as part of the Precision in Psychiatry (PIP) study (21), an observational, longitudinal study in which participants underwent a four-week course of iCBT or antidepressant medication. Further details of the PIP study procedures and ethical approval can be found in a prior publication (21). A power analysis was carried out using effect sizes from a previous study examining cross-sectional associations between metacognition and anxious-depression, and compulsivity and intrusive thought (7). Sample sizes of N=454 and N=332 respectively were required to detect these associations with 80% power. The sample sizes of the antidepressant arm and control group were smaller and used for secondary and more exploratory analyses.

iCBT Arm. Individuals initiating iCBT provided by SilverCloud Health were recruited from two sites: 1) the National Health Service Berkshire Foundation in the UK and 2) Aware mental health charity in Ireland. Participants included in the study either started their iCBT intervention ≤2 days prior to signing up, or provided a treatment start date in the near future, and scored ≥10 on the Work and Social Adjustment Scale (WSAS) at baseline, which indicated significant functional impairment due to clinical symptoms (34). Figure 1A shows the disposition of participants throughout the study. N=2404 were screened, of whom N=1496 were eligible, N=836 completed baseline assessments and met inclusion criteria (detailed in the Supplement). A final N=649 completed and met inclusion criteria for follow-up assessments. While study follow-up data was collected after four weeks of treatment, iCBT could last up to 12 weeks (21). The final sample was, on average, 32.2 years old (SD=11.0), mostly female (n=501, 77.4%), living in the United Kingdom (n=546, 84.4%), and had some or completed undergraduate level education (n=342, 52.9%) (Table S1).

Antidepressant Arm. Individuals were recruited globally using advertisements placed on Google search, in addition to social media platforms, mental health websites, local pharmacies and General Practitioner waiting rooms. Participants were included if they started or planned to start treatment ≤2 days of study sign-up, scored ≥10 on the WSAS at baseline, and provided a valid photograph of an antidepressant medication prescription. N=270 individuals were screened, of whom N=174 were eligible, N=102 completed and met inclusion criteria at baseline and a final N=82 had follow-up data (Figure 1A). Participants were mostly female (n=60, 73.2%), mean age=30.5 (10.5), were living in Ireland or the United Kingdom (n=66, 80.5%) and had some or completed undergraduate level education (n=49, 59.8%) (Table S1).

Control Group. Participants in the no treatment control group were recruited through university mailings lists and advertisements posted online and around Trinity

College Dublin. Participants included in this arm scored <10 on an adapted version of the WSAS (where they rated functional impairment from their general problems rather than mental health problems) and self-reported that they had no current mental health problems and were not undergoing treatment for any mental health problems at the time of screening. N=444 individuals were screened, of whom N=245 were eligible, N=113 had baseline data and a final N=88 completed follow-up assessments and met inclusion criteria for the study (Figure 1A). Participants in the control group were matched for sociodemographic characteristics in the antidepressant arm at screening (Table S1), further detailed in the Supplement.

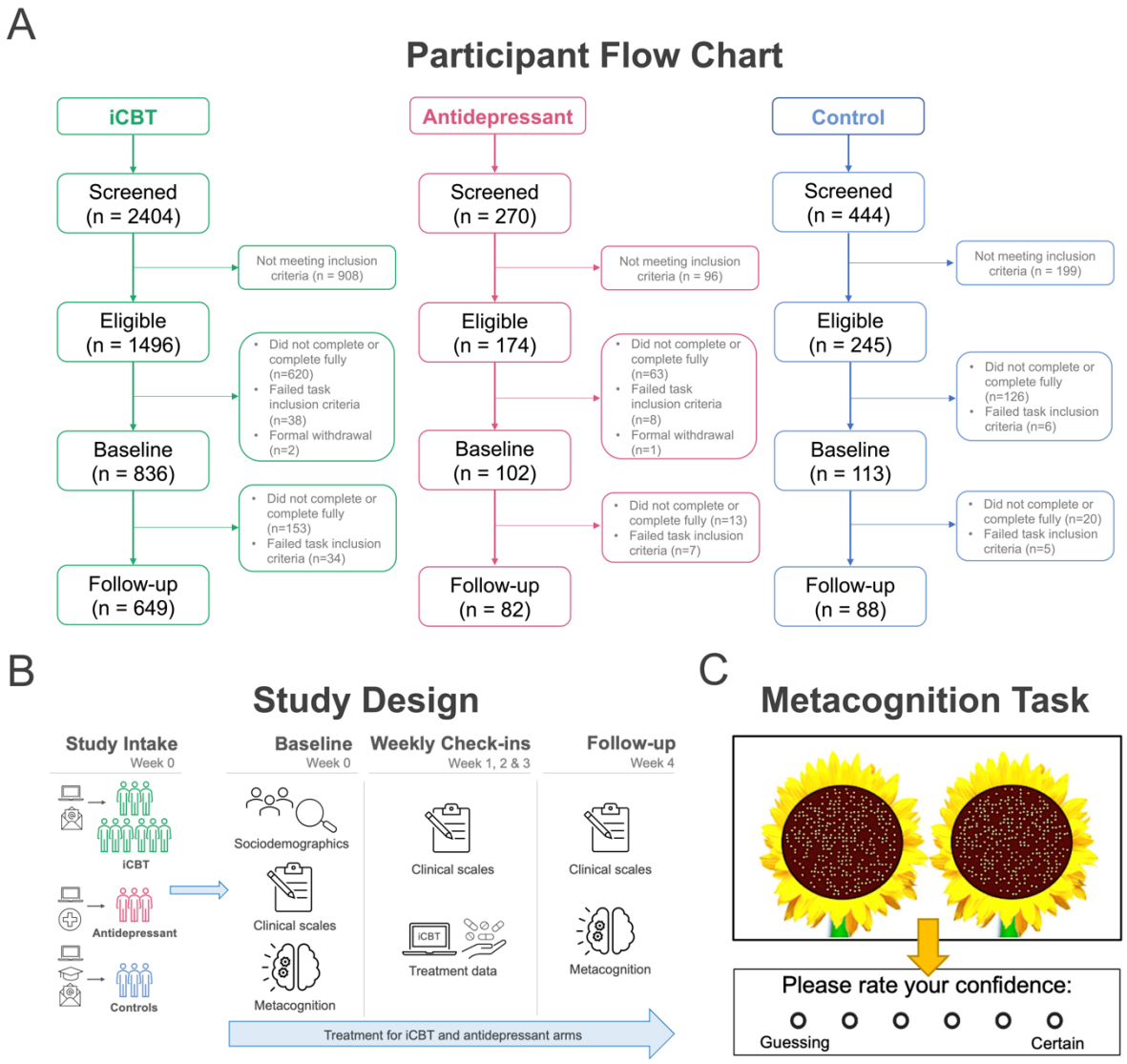

Figure 1. (A) Participant flow chart (CONSORT chart). Participants were considered 'completers' if they had metacognitive and transdiagnostic psychiatric dimension data at baseline and follow-up and met task inclusion criteria. (B) Overview of study design from study intake (week 0) to follow-up (week 4) assessments across groups. (C) Metacognitive (visuo-perceptual decision-making) task design (N = 210 trials). On each trial, participants were asked to judge and choose the sunflower that contained more seeds (i.e., higher number of dots) and then provide a confidence rating on their decision.

Procedure

Figure 1B shows an overview of the study design, including the assessments involved at each timepoint. For the purposes of this study, we focused on a select set of sociodemographic characteristics (gender, age, country of residence, level of educational attainment), self-reported psychiatric questionnaires, metacognitive task performance and treatment data from the PIP study (21).

Self-Reported Psychiatric Questionnaires. Participants completed nine self-report questionnaires at baseline and follow-up that assess a variety of psychiatric symptoms (see Supplement for questionnaire details).

Metacognitive Task. Participants completed a visuo-perceptual decision-making task (26) to assess metacognition (Figure 1C). On each of the 210 trials, participants were asked to judge and choose the sunflower that contained more seeds (i.e., higher number of dots) and then provide a confidence rating on their decision. Mean accuracy was tightly controlled in this task using a 'two-down one-up' staircase procedure, in which equal changes in dot difference occurred after each incorrect response and after two consecutive correct responses, detailed further in the Supplement.

Treatment Data. Objective indicators of treatment engagement were provided by SilverCloud for 640 participants in the iCBT arm, which comprised of percentage of program viewed, time (minutes) spent in the program, and program type (listed in the Supplement). Information on concurrent treatment and treatment adherence across each group are reported in the Supplement.

Data Preparation and Analysis

Questionnaire Data. Individual scores on dimensions of anxious-depression, compulsivity and intrusive thought, and social withdrawal were calculated by multiplying each of the 209 item scores on the nine self-report clinical scales by the 209 corresponding item weights from a previously published factor analysis on these scales (35). Dimension scores were then scaled to centre on zero, with higher scores indicating higher levels of transdiagnostic psychopathology. We additionally tested for consistency in the factor structure in this dataset by carrying out a factor analysis on these items and testing their correlation with the prior work in unselected samples (reported in the Supplement). Careless or inattentive responding to questionnaires was detected with embedded 'catch' items across questionnaires, detailed in the Supplement.

Metacognition Task. The perceptual decision-making task performance was used to quantify our primary cognitive outcome measure, metacognitive bias, the mean confidence rating across trials. Other task measures include mean dot difference (task difficulty), mean accuracy and mean reaction time (in seconds), which are described further in the Supplement. As metacognitive efficiency was not previously associated with transdiagnostic dimensions cross-sectionally (7,9,11), results pertaining to efficiency are reported separately in the Supplement.

Statistical Analysis. We tested for relationships between baseline task measures

and the psychiatric symptom dimensions using linear regression analysis, controlling for age, gender, and education. To examine pre-post changes, we carried out linear mixed-effects models with measures of metacognition or psychopathology as the dependent variable, time (baseline=0; follow-up=1) as the independent variable and participants as random effects. To determine the association between change in confidence and change in anxious-depression, we used Pearson correlation analyses. Exploratory linear regression analyses tested the specificity of the effects, replacing anxious-depression with each of the measures of psychopathology in turn as follows: Mean confidence ~ time*dimension/psychiatric scale score. We additionally ran regression analyses to test if concurrent treatment or the degree of objective engagement in iCBT interacted with the effect of time on mean confidence. Exploratory ANOVA analyses were also conducted to compare changes in anxious-depression, task difficulty and confidence across the three arms directly. For all tests, statistical significance was defined as $p<0.05$, with two-tailed p-values used. All regressors were scaled as Z scores to compare the regression coefficients of independent variables within each model. For exploratory regression analyses, adjustments for multiple comparisons were not conducted (36). The code and data to reproduce statistical analyses are available at https://osf.io/89xzq/.

RESULTS

Cross-sectional Findings at Baseline: iCBT

At baseline, participants with higher levels of anxious-depression had lower levels of mean confidence (β=-0.09, SE=0.03, p=0.008; Figure 2A & 2B), while those with higher levels of compulsivity and intrusive thought had elevated mean confidence (β=0.11, SE=0.03, p=0.002; Figure 2A & 2C), controlling for age, gender, and education. Levels of social withdrawal were not associated with mean confidence (β=-0.05, SE=0.03, p=0.168; Figure 2A).

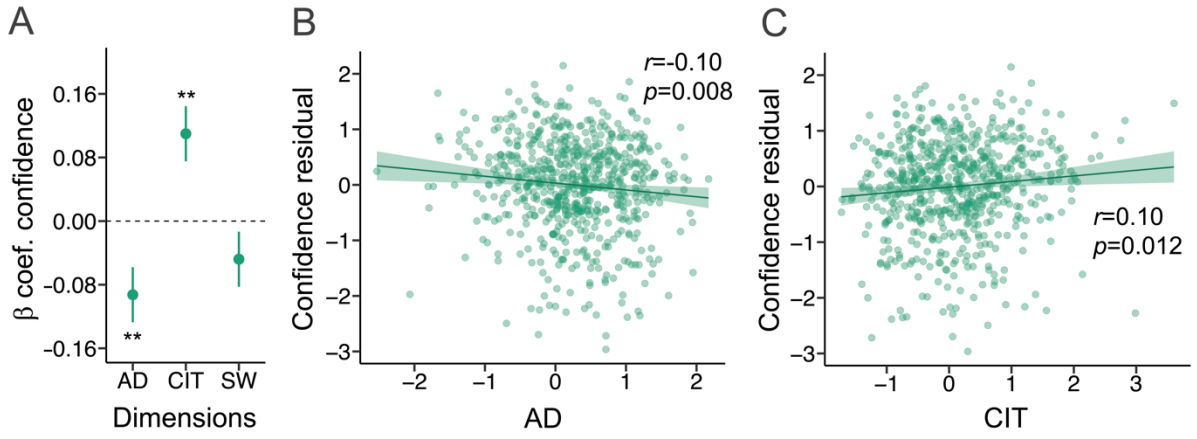

FIGURE 2. β = standardised beta coefficient, *r* = correlation coefficient, *p* = p-value, AD = Anxious-Depression, CIT = Compulsivity and Intrusive Thought, SW = Social Withdrawal. (A) AD and CIT were associated with metacognitive bias, while SW was not. The residual values for confidence (controlling for age, gender and education) were negatively associated with AD. (C) The residual values for confidence (controlling for age, gender and education) were positively associated with CIT.

Treatment Findings: iCBT

The transdiagnostic dimensions and psychiatric scale scores all significantly improved from baseline to four-week follow-up, except for impulsivity (Figure 3A, Table S2). In tandem with these clinical changes, there was a small but significant increase in mean confidence from baseline (M=3.78, SD=0.85) to follow-up (M=3.95, SD=0.89), (β=0.17, SE=0.02, p<0.001, r^2=0.01) (Figure 3B). Performance accuracy improved, which due to the staircasing calibration was reflected as increased task difficulty from baseline (dot difference: M=41.82, SD=11.61) to follow-up (dot difference: M=39.80, SD=12.62), (β=-2.02, SE=0.44, p<0.001, r^2=0.01) (Figure 3C). Additionally, the effect of time on confidence was not dependent on how much participants engaged in iCBT, as indexed by time spent in the program (β<0.01, SE<0.01, p=0.756) and percentage of the iCBT program viewed (β=0.09, SE=0.21, p=0.650). Change in confidence was also not dependent on receiving concurrent treatment (β=-0.03, SE=0.06, p=0.566), with 175 participants (27.0%) in the iCBT group receiving another treatment during the study (further detailed in the Supplement).

Importantly, change in anxious-depression was significantly associated with change in confidence (r(647)=-0.12, p=0.002), such that those with the largest decrease in anxious-depression had the greatest increase in confidence (Figure 3D). Change in confidence was not significantly associated with change in compulsivity and intrusive thought (r(647)=-0.05, p=0.211). The relationship between change in anxious-depression and change in task difficulty was not significant (r(647)=0.01, p=0.835). A significant interaction effect of time and anxious-depression on mean confidence held when including change in compulsivity and intrusive thought and change in social withdrawal as covariates in the model (β=-0.07, SE=0.03, p=0.005). There was no significant interaction effect of time and baseline confidence (β=0.06, SE=0.04, p=0.144) or an interaction effect of time and baseline anxious-depression (β=-0.03, SE=0.05, p=0.611) on mean confidence. Exploratory analyses determined the specificity of these effects to anxious-depression by examining the interaction effect of time and change in each psychiatric score on mean confidence. Changes in trait anxiety (β=-0.08, SE=0.02, p=0.002), depression (β=-0.06, SE=0.02 p=0.011) and alcohol misuse (β=-0.05, SE=0.02, p=0.037) also showed an association with changes in confidence (Figure 3E and Table S3).

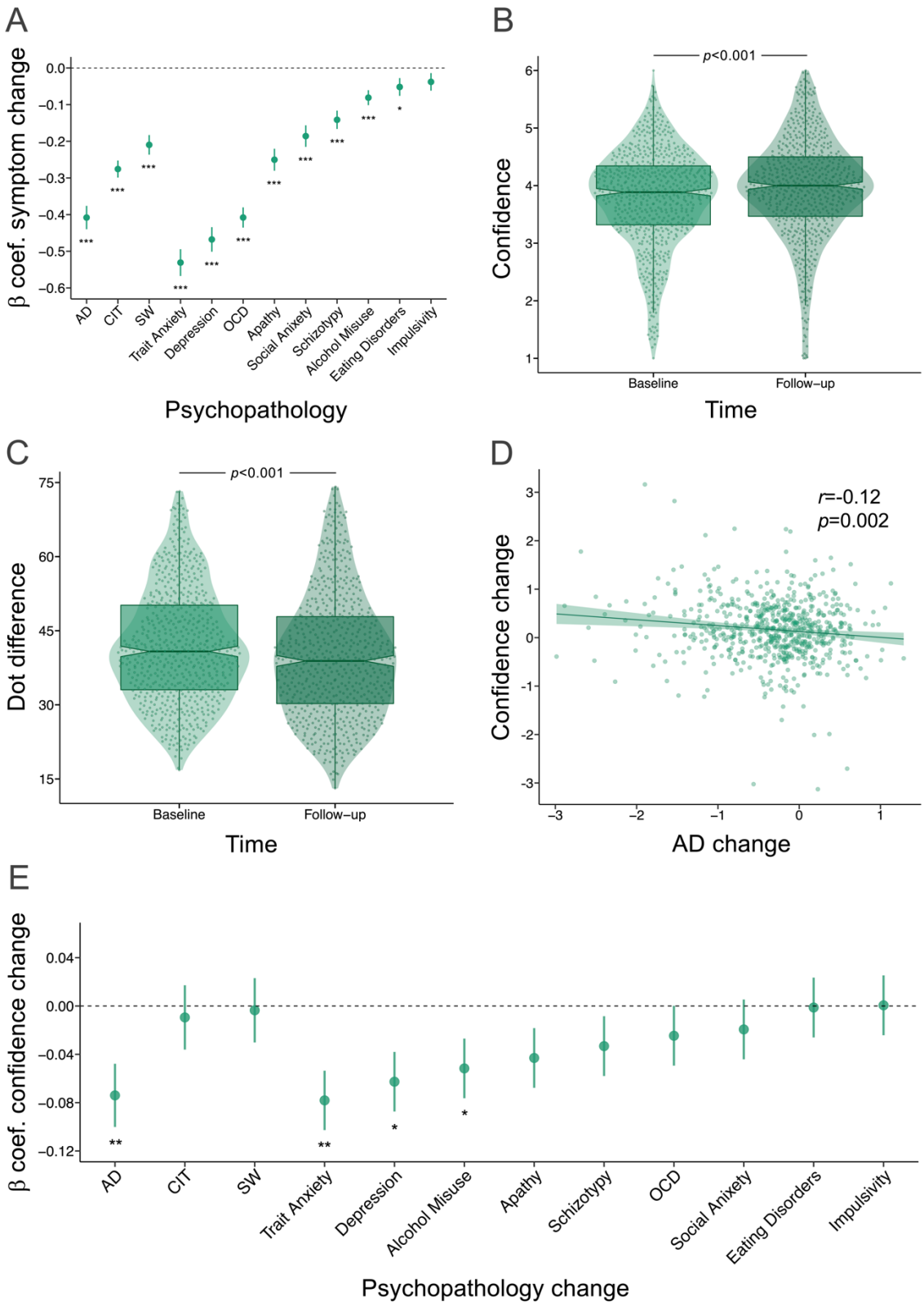

FIGURE 3. β = standardised beta coefficient, AD = Anxious-Depression, CIT = Compulsivity and Intrusive Thought, SW = Social Withdrawal, OCD = Obsessive compulsive disorder, *r* = correlation coefficient, *p* = p-value (unadjusted), *** = *p*<0.001, ** = *p*<0.01, * = *p*<0.05. (A) Psychopathology symptoms improved with four weeks of iCBT. (B) Confidence was significantly higher and, (C) the task was more difficult at four-week follow-up. (D) Those with the largest improvements in AD had the greater increases in confidence. (E) Change in confidence also scaled with improvements in trait anxiety, depression and alcohol misuse.

Comparing iCBT, Antidepressant and Control Groups

Examining simple effects in the antidepressant arm, there was a significant reduction in anxious-depression from baseline to follow-up (β=-0.61, SE=0.09, p<0.001). Among controls, levels of anxious-depression did not significantly change (β=0.10, SE=0.06, p=0.096). Further details of transdiagnostic clinical changes for the antidepressant and controls groups are presented in Figure 4A and Table S4. When comparing the three groups directly, ANOVA analysis predicting anxious-depression scores with group and time as independent variables revealed a main effect of time (F(1, 1632)=62.99, p<0.001), a main effect of group (F(2, 1632)=249.74, p<0.001), and an interaction effect of group and time (F(2, 1632)=9.23, p<0.001).

With respect to confidence, tests of simple effects revealed that mean confidence significantly increased from baseline (M=3.77, SD=0.88) to follow-up (M=4.07, SD=0.79) in the antidepressant arm (β=0.31, SE=0.08, p<0.001) (Figure 4B). Among controls, there was no significant change in confidence from baseline (M=3.68, SD=0.86) to follow-up (M=3.79, SD=0.92) (β=0.11, SE=0.07, p=0.103), though it went in the same direction (Figure 4B). Predicting confidence scores using ANOVA analysis with group and time as independent variables revealed a main effect of time (F(1, 1632)=16.26, p<0.001), and no significant main effect of group (F(2, 1632)=2.35, p=0.096). The interaction effect of group and time on mean confidence was not significant (F(2, 1632)=0.60, p=0.550), suggesting that change in confidence did not differ across the three groups.

In the antidepressant arm, mean dot difference decreased from baseline (M=41.2, SD=13.3) to follow-up (M=35.3, SD=13.1) (β=-5.91, SE=1.25, p<0.001), indicating increased task difficulty. There was no significant change in task difficulty among controls from baseline (M=43.0, SD=11.8) to follow-up (M=41.4, SD=13.6) (β=-1.64, SE=1.30, p=0.210) (Figure 4C). With the three groups in the model, there was a significant main effect of time (F(1, 1632)=15.17, p=0.001) and group (F(2, 1632)=4.56, p=0.011) on mean dot difference. The interaction effect of time and group on mean dot difference was not significant (F(2, 1632)=1.91, p=0.148), suggesting no differences across the groups in task difficulty changes.

While our sample was underpowered to examine individual differences, we conducted an exploratory analysis examining the connection between changes in anxious-depression symptoms and changes in confidence in the antidepressant and controls groups. Although not significant, the association between change in confidence and change in anxious-depression was in the expected negative direction in the antidepressant arm (r(80)=-0.10, p=0.381), and among controls (r(86)=-0.17, p=0.111) (Figure 4D). When examining the effects of time, group and anxious-depression change on mean confidence, there was a significant interaction effect of time and anxious-depression change on mean confidence (F(1, 1626)=4.04, p=0.045), suggesting change in confidence was dependent on change in anxious-depression. There was no significant three-way interaction of anxious-depression change, time and group on mean confidence when comparing the three groups (F(2, 1626)=0.08, p=0.928), indicating that the significant association between confidence change and anxious-depression change was not specific to any group.

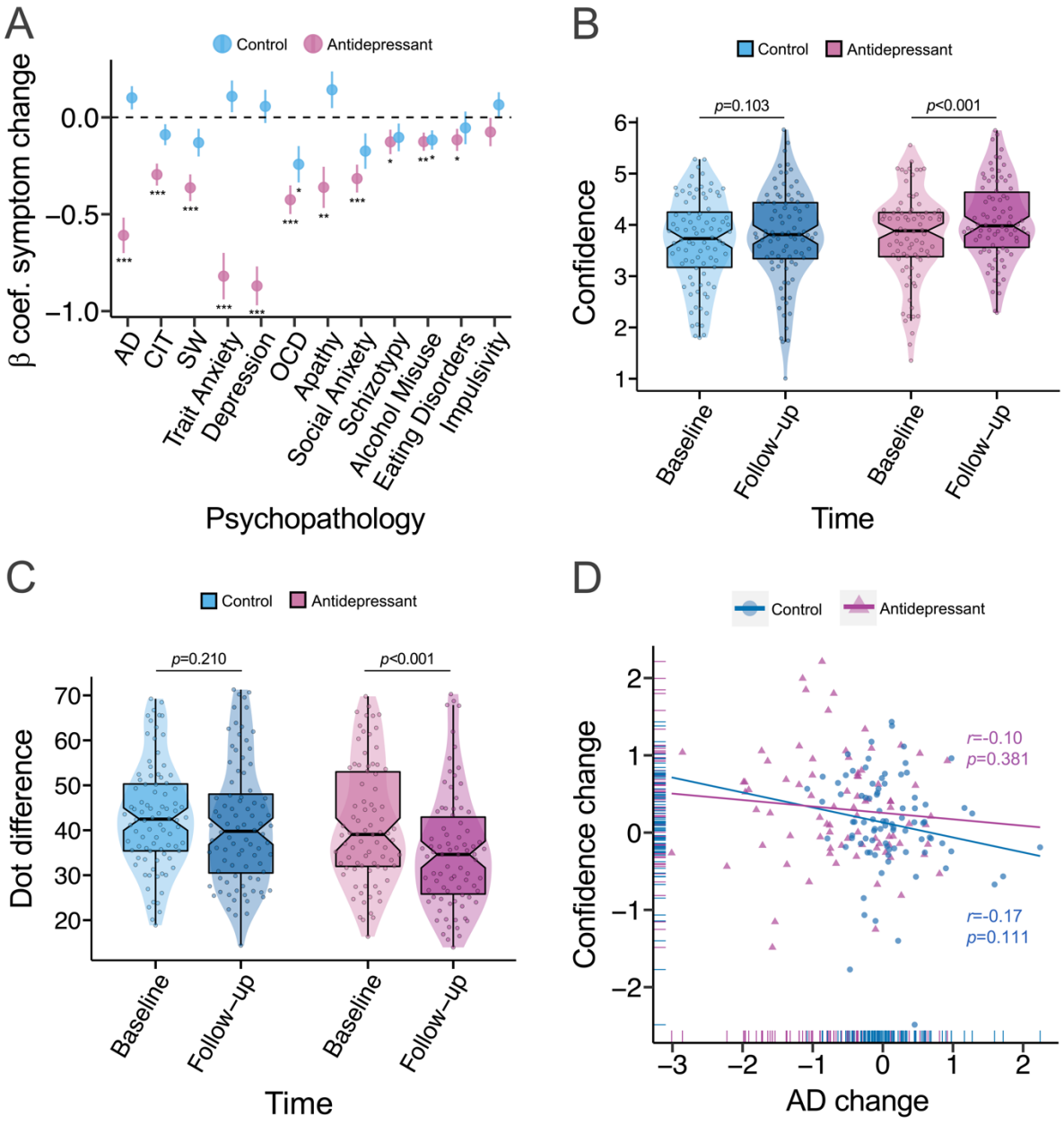

FIGURE 4. β = standardised beta coefficient, AD = Anxious-Depression, CIT = Compulsivity and Intrusive Thought, SW = Social Withdrawal, OCD = Obsessive compulsive disorder, *r* = correlation coefficient, *p* = p-value, *** = p<0.001, ** = p<0.01, * = p<0.05. (A) The majority of psychiatric scales improved in the antidepressant arm after 4 weeks of treatment, while the controls only had significant reductions in OCD symptoms and alcohol misuse at follow-up. (B) The larger increase in confidence in the antidepressant arm compared to controls was trended towards significant. (C) The antidepressant arm had a greater increase in task difficulty (a reduction in dot difference across stimuli) from baseline to follow-up, relative to controls. (D) Although not significant, the association between change in confidence and change in anxious-depression was in the expected negative direction in the antidepressant arm and among controls.

DISCUSSION

Metacognitive biases are linked to transdiagnostic dimensions of mental health, but it is presently unclear if these biases are stable traits, or if they fluctuate alongside symptoms and change during the course of treatment (10). To answer these questions, we administered a previously validated adaptive task of metacognitive ability that controls for objective performance differences (26) in a large sample of individuals before and after four weeks of iCBT or antidepressant medications (21). As expected, a four-week course of iCBT or antidepressant medication led to transdiagnostic improvements in mental health (27–29). Alongside this, there was a significant increase in metacognitive confidence following four weeks of iCBT or antidepressant medication. Not simply a practice effect, we found that individuals in the iCBT arm with the greatest improvements in anxious-depression had the largest increase in confidence at follow-up. These findings suggest that metacognitive biases in anxious-depression are state-dependent. This builds on previous findings in small samples that have shown iCBT improves self-reported metacognitive self-beliefs (25) and that metacognition can be altered through adaptive training (12–15).

At baseline, we replicated the previously observed bi-directional associations between metacognitive bias and anxious-depression and compulsivity and intrusive thought (7–9,11). While higher levels of anxious-depression is associated with lower confidence, those with higher levels of compulsivity and intrusive thought have elevated confidence. This is a somewhat surprising dissociation, as compulsivity and anxious-depression are themselves positively correlated in the population. One way this can be reconciled is if the mechanisms underlying these opposing confidence biases are distinct. In anxious-depression, there appears to be more pervasive metacognitive biases that affect confidence in many domains and levels of a metacognitive hierarchy (spanning confidence in low level perceptual decisions to ideas of self-worth) (9,10). In contrast, inflated confidence in compulsivity may be based on more specific biases in learning and inference (8).

The present study was observational and therefore did not randomly assign participants to a different treatments. To partially remediate that limitation, we included two smaller groups receiving antidepressant medication and a control group. Levels of transdiagnostic psychiatric dimensions remained stable across time among controls, while they significantly improved in the antidepressant arm. Similarly to iCBT, we found that confidence improved in the antidepressant group, but not among controls. The interaction, however, was not significant, meaning that we cannot reject the null hypothesis that confidence improved to the same degree across the three groups. As increased task difficulty among clinical groups was not significantly greater relative to controls, changes in task difficulty may simply reflect greater task familiarity at follow-up across groups, as opposed to gains in general perceptual performance among clinical arms. Examining the three groups together, the data suggests that confidence changes are unlikely to be treatment specific, rather, confidence fluctuates in tandem with anxious-depression. This was evident in an overall association between change in anxious-depression and change in confidence that was not modified by treatment arm. Additionally, levels of iCBT engagement and concurrent treatments did not bolster changes in confidence. Overall, the results indicated that metacognition fluctuates with anxious-depression state, regardless of treatment type or exposure. Future research with larger samples

are required to address this definitively.

Limitations and Future Directions

Confidence change and anxious-depression change were significantly but weakly associated. Similarly, the relative change in confidence across treatment arms was small. Therefore, while tests of metacognitive confidence can inform theoretical models, like most cognitive tests, they are likely of limited utility in clinical practice, at least when used in isolation (19). Given the complexity of mental health causes and presentations, multivariable models are needed to see practical value from such tests. We did not assess confidence or anxious-depression to treatment cessation and so the causal path and temporal dependence, if they exist, cannot be derived from these data. Future research should consider assessing metacognition and anxious-depression continuously through treatment, in order to elucidate the causal relationship between anxious-depression and metacognition with mediation analysis (25). While this study examined changes in metacognition with iCBT generally, future research should examine if the strength of the association between confidence change and anxious-depression change is greater following iCBT modules targeting metacognition or following metacognitive intervention (4). The iCBT programs in this study primarily targeted depression and anxiety, which may explain why changes in confidence did not scale with improvements in compulsivity. Future research is required to assess if treatments aimed at compulsive disorders decrease the over-confidence commonly observed in those high in compulsivity and intrusive thought. As the antidepressant and control groups were much smaller than the iCBT arm, we were unable to compare changes in confidence across the types of antidepressant medications individuals received and we were underpowered more generally for individual differences analyses and multi-arm comparisons. Exploratory analyses were nonetheless presented and can form the basis for future investigations.

Conclusions

Our findings replicated the cross-sectional evidence that higher levels of anxious-depression are associated with under-confidence. We demonstrate that metacognitive confidence increases following four weeks of iCBT or antidepressant treatment. Overall, we observed that the greater the improvement in anxious-depression, the more confident participants became, which did not appear to be dependent on treatment type. This suggests that metacognitive biases in anxious-depression are state-dependent and might be normalised through clinical improvements.

REFERENCES

1. Fleming SM, Lau HC. How to measure metacognition. Front Hum Neurosci. 2014;8:443.

2. Fleming SM, Daw ND. Self-evaluation of decision-making: a general bayesian framework for metacognitive computation. Psychol Rev. 2017;124(1):91–114.

3. Fleming SM, Dolan RJ, Frith CD. Metacognition: computation, biology and function. Philos Trans R Soc Lond B Biol Sci. 2012;367(1594):1280–6.

4. Philipp R, Kriston L, Kühne F, Härter M, Meister R. Concepts of metacognition in the treatment of patients with mental disorders. J Ration-Emotive Cogn-Behav Ther. 2020;38(2):173–83.

5. Hoven M, Lebreton M, Engelmann JB, Denys D, Luigjes J, van Holst RJ. Abnormalities of confidence in psychiatry: an overview and future perspectives. Transl Psychiatry. 2019;9(1):268.

6. Wise T, Robinson O, Gillan C. Identifying transdiagnostic mechanisms in mental health using computational factor modeling [Internet]. Biol Psychiatry [Pre-proof]. 2022 [cited 2022 Oct 10];0(0). Available from: https://www.biologicalpsychiatryjournal.com/article/S0006-3223(22)01661-4/fulltext

7. Rouault M, Seow T, Gillan CM, Fleming SM. P Psychiatric symptom dimensions are associated with dissociable shifts in metacognition but not task performance. Biol Psychiatry. 2018;84(6):443–51.

8. Seow TXF, Gillan CM. Transdiagnostic phenotyping reveals a host of metacognitive deficits implicated in compulsivity. Sci Rep. 2020;10(1):2883.

9. Hoven M, Denys D, Rouault M, Luigjes J, Holst R van. How do confidence and self-beliefs relate in psychopathology: a transdiagnostic approach [Internet]. PsyArXiv; 2022 [cited 2022 Aug 22]. Available from: https://psyarxiv.com/d45gn/

10. Seow TXF, Rouault M, Gillan CM, Fleming SM. How local and global metacognition shape mental health. Biol Psychiatry. 2021;90(7):436–46.

11. Benwell CSY, Mohr G, Wallberg J, Kouadio A, Ince RAA. Psychiatrically relevant signatures of domain-general decision-making and metacognition in the general population. Npj Ment Health Res. 2022;1(1):1–17.

12. Carpenter J, Sherman MT, Kievit RA, Seth AK, Lau H, Fleming SM. Domain-general enhancements of metacognitive ability through adaptive training. J Exp Psychol Gen. 2019;148(1):51–64.

13. Engeler NC, Gilbert SJ. The effect of metacognitive training on confidence and strategic reminder setting. PloS One. 2020;15(10):e0240858.

14. Jelinek L, Van Quaquebeke N, Moritz S. Cognitive and metacognitive mechanisms of change in metacognitive training for depression. Sci Rep. 2017;7(1):3449.

15. Lysaker PH, Gagen E, Moritz S, Schweitzer RD. Metacognitive approaches to the treatment of psychosis: a comparison of four approaches. Psychol Res Behav Manag. 2018;11:341–51.

16. Eisenacher S, Rausch F, Ainser F, Mier D, Veckenstedt R, Schirmbeck F, et al. Investigation of metamemory functioning in the at-risk mental state for psychosis. Psychol Med. 2015;45(15):3329–40.

17. Gawęda Ł, Li E, Lavoie S, Whitford TJ, Moritz S, Nelson B. Impaired action self-monitoring and cognitive confidence among ultra-high risk for psychosis and first-episode psychosis patients. Eur Psychiatry J Assoc Eur Psychiatr. 2018;47:67–75.

18. Moeller SJ, Fleming SM, Gan G, Zilverstand A, Malaker P, d'Oleire Uquillas F, et al. Metacognitive impairment in active cocaine use disorder is associated with individual differences in brain structure. Eur Neuropsychopharmacol. 2016;26(4):653–62.

19. Mogoașe C, Cobeanu O, David O, Giosan C, Szentagotai A. Internet-based psychotherapy for adult depression: what about the mechanisms of change? J Clin Psychol. 2017;73(1):5–64.

20. Webb CA, Rosso IM, Rauch SL. Internet-based cognitive-behavioral therapy for depression: current progress and future directions. Harv Rev Psychiatry. 2017;25(3):114–22.

21. Lee CT, Palacios J, Richards D, Hanlon AK, Lynch K, Harty S, et al. The Precision in Psychiatry (PIP) study: Testing an internet-based methodology for accelerating research in treatment prediction and personalisation. BMC Psychiatry. 2023;23(1):25.

22. Andersson G, Carlbring P, Rozental A. Response and remission rates in internet-based cognitive behavior therapy: an individual patient data meta-analysis. Front Psychiatry. 2019;10:749.

23. Eilert N, Enrique A, Wogan R, Mooney O, Timulak L, Richards D. The effectiveness of Internet-delivered treatment for generalized anxiety disorder: An updated systematic review and meta-analysis. Depress Anxiety. 2021;38(2):196–219.

24. Karyotaki E, Efthimiou O, Miguel C, Bermpohl FMG, Furukawa TA, Cuijpers P, et al. Internet-based cognitive behavioral therapy for depression: a systematic review and individual patient data network meta-analysis. JAMA Psychiatry. 2021;78(4):361–71.

25. Newby JM, Williams AD, Andrews G. Reductions in negative repetitive thinking and metacognitive beliefs during transdiagnostic internet cognitive

behavioural therapy (iCBT) for mixed anxiety and depression. Behav Res Ther. 2014;59:52–60.

26. Fleming SM, Ryu J, Golfinos JG, Blackmon KE. Domain-specific impairment in metacognitive accuracy following anterior prefrontal lesions. Brain. 2014;137(10):2811–22.

27. Cipriani A, Furukawa TA, Salanti G, Chaimani A, Atkinson LZ, Ogawa Y, et al. Comparative efficacy and acceptability of 21 antidepressant drugs for the acute treatment of adults with major depressive disorder: a systematic review and network meta-analysis. Lancet Lond Engl. 2018;391(10128):1357–66.

28. Gøtzsche PC, Dinnage O. What have antidepressants been tested for? A systematic review. Int J Risk Saf Med. 2020;31(3):157–63.

29. Skapinakis P, Caldwell DM, Hollingworth W, Bryden P, Fineberg NA, Salkovskis P, et al. Pharmacological and psychotherapeutic interventions for management of obsessive-compulsive disorder in adults: a systematic review and network meta-analysis. Lancet Psychiatry. 2016;3(8):730–9.

30. Prado CE, Watt S, Crowe SF. A meta-analysis of the effects of antidepressants on cognitive functioning in depressed and non-depressed samples. Neuropsychol Rev. 2018;28(1):32–72.

31. Rosenblat JD, Kakar R, McIntyre RS. The cognitive effects of antidepressants in major depressive disorder: a systematic review and meta-analysis of randomized clinical trials. Int J Neuropsychopharmacol. 2015;19(2):pyv082.

32. Salagre E, Solé B, Tomioka Y, Fernandes BS, Hidalgo-Mazzei D, Garriga M, et al. Treatment of neurocognitive symptoms in unipolar depression: A systematic review and future perspectives. J Affect Disord. 2017;221:205–21.

33. Vernon JA, Grudnikoff E, Seidman AJ, Frazier TW, Vemulapalli MS, Pareek P, et al. Antidepressants for cognitive impairment in schizophrenia--a systematic review and meta-analysis. Schizophr Res. 2014;159(2–3):385–94.

34. Mundt JC, Marks IM, Shear MK, Greist JH. The Work and Social Adjustment Scale: a simple measure of impairment in functioning. Br J Psychiatry J Ment Sci. 2002;180:461–4.

35. Gillan CM, Kosinski M, Whelan R, Phelps EA, Daw ND. Characterizing a psychiatric symptom dimension related to deficits in goal-directed control. eLife. 2016;5:e11305.

36. Althouse AD. Adjust for multiple comparisons? It's not that simple. Ann Thorac Surg. 2016;101(5):1644–5.