

Emotional and interpersonal mechanisms in community SSRI treatment of social anxiety disorder

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Published online on Oct. 7, 2020; subject to revision

Background: Affective and interpersonal behavioural patterns characteristic of social anxiety disorder show improvement during treatment with serotonin agonists (e.g., selective serotonin reuptake inhibitors), commonly used in the treatment of social anxiety disorder. The present study sought to establish whether, during community psychopharmacological treatment of social anxiety disorder, changes in positive or negative affect and agreeable or quarrelsome behaviour mediate improvement in social anxiety symptom severity or follow from it. **Methods:** Adults diagnosed with social anxiety disorder ($n = 48$) recorded their interpersonal behaviour and affect naturalistically in an event-contingent recording procedure for 1-week periods before and during the first 4 months of treatment with paroxetine. Participants and treating psychiatrists assessed the severity of social anxiety symptoms monthly. A multivariate latent change score framework examined temporally lagged associations of change in affect and interpersonal behaviour with change in social anxiety symptom severity. **Results:** Elevated agreeable behaviour and positive affect predicted greater subsequent reduction in social anxiety symptom severity over the following month of treatment. Elevated negative affect, but not quarrelsome behaviour, predicted less subsequent reduction in symptom severity. **Limitations:** Limitations included limited assessment of extreme behaviour (e.g., violence) that may have precluded examining the efficacy of paroxetine because of the lack of a placebo control group. **Conclusion:** The present study suggests that interpersonal behaviour and affect may be putative mechanisms of action for serotonergic treatment of social anxiety disorder. Prosocial behaviour and positive affect increase during serotonergic treatment of social anxiety disorder. Specifically, modulating agreeable behaviour, positive affect and negative affect in individuals' daily lives may partially explain and refine clinical intervention.

Introduction

Social anxiety disorder (also known as social phobia) describes a syndrome of characteristic physiologic, affective, cognitive and behavioural responses that reflect persistent anxiety related to social or interpersonal situations. Within the cognitive-behavioural formulation, anticipation and interpretation of negative social outcomes contribute to elevated anxiotypic physiologic and affective responses. For example, the diagnostic criteria for social anxiety disorder describe fear that one will be negatively evaluated in social interactions with others.¹ Through limiting social interaction, interpersonal behaviours reduce exposure to anticipated negative evaluation and may provide temporary relief from attendant social anxiety.² Over time, persistent anxiety may lead individuals with social anxiety disorder to develop a greater sensitivity to anxiotypic responses,³ which could increase avoidance of social situations. However, interpersonal behaviour (e.g., quarrelsome behaviour)

may beget negative responses (e.g., quarrelsome behaviour) from others.⁴ Thus, interpersonal behaviours that limit social interaction may also increase the likelihood of negative social outcomes, including feared negative social evaluation.

Serotonergic medications (e.g., selective serotonin reuptake inhibitors [SSRIs]) have demonstrated effectiveness in treating social anxiety disorder in adults^{5,6} and currently comprise first-line pharmacological treatment for social anxiety disorder.^{7,8} However, specific mechanisms by which SSRI medications ameliorate social anxiety disorder symptoms are largely unknown. Consistent with broad interest in mechanisms of action,⁹ a growing body of research examines putative biological, neural and psychological targets that may explain the anxiolytic effects of SSRI medications.¹⁰ Administration of SSRIs to adults with social anxiety disorder may modulate specific physiologic, cognitive, affective and interpersonal patterns that contribute to the maintenance of social anxiety disorder. For example, research with community adults and

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Submitted Sep. 30, 2019; Revised Apr. 4, 2020; Accepted Apr. 6, 2020

DOI: 10.1503/jpn.190164

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with nonhuman primates¹¹ demonstrated that serotonin modulation — such as through the administration of tryptophan,^{12,13} SSRIs¹⁴ or selective serotonin and norepinephrine reuptake inhibitors^{15,16} — is associated with increased communal (e.g., agreeable) behaviour,^{17,18} increased dominant behaviour¹⁹ and decreased aggression.²⁰

Two theories, the Social Interaction Model and the Cognitive Neuropsychological Model, implicate serotonergic regulation in cognitive, affective and interpersonal processes. Although they identify different putative mechanisms, both theories suggest that improvements in characteristic cognitive, affective or interpersonal processes may mediate and explain the well-documented effectiveness of serotonergic medications. As proposed by Young and colleagues,²¹ the Social Interaction Model suggests that serotonergic medications increase prosocial behaviour and decrease behavioural variability, which subsequently improves the quality of a person's interpersonal interactions and social relationships. Alternatively, the Cognitive Neuropsychological Model, proposed by Harmer and colleagues,^{22,23} suggests that serotonergic and norepinephrine medications facilitate changes in cognitive processing (e.g., attention and memory), ameliorating deficits previously implicated in multiple anxiety disorders.

Existing research describes psychological (i.e., cognitive, affective, behavioural) and neural correlates of serotonergic pharmacotherapy, but further research is needed to identify whether changes in psychological function follow from or precede and influence subsequent improvements. Statistical innovations can distinguish between these 2 scenarios. The latent difference score (also known as the latent change score) framework leverages structural equation modelling to examine change over time and lagged associations of absolute level and change in multiple processes over time.^{24,25} For example, Hawley and colleagues²⁶ used a latent difference score model to find that higher monthly perfectionism predicted less subsequent reduction in symptom severity over the following month of psychotherapy for major depressive disorder.

Extant research has been largely limited to self-report and laboratory-based assessment of change in psychological processes. Although laboratory-based assessment is well suited to the study of specific cognitive, affective and neural processes, examination of the social aspects of social anxiety disorder indicates the need to clarify the naturalistic manifestation of psychological processes in individuals' daily lives. Ecological momentary assessment and related methodologies provide high temporal density assessments taken during participants' daily lives.²⁷ These methodologies are appropriate for clarifying the naturalistic manifestation of psychological processes in diverse real-world contexts relevant to the interpersonal problems critical to social anxiety disorder. For example, ecological momentary assessment research identified replicable dynamics of affect²⁸ and interpersonal behaviour²⁹ that predict later functional impairment.^{30,31} Moreover, temporal patterns derived from ecological momentary assessments provide enhanced reliability³² and are not as influenced by traditional limitations of self-report, such as recall bias.³³

The present study presents secondary data analysis of a study that demonstrated improvement in specific affective and behavioural patterns characteristic of social anxiety disorder (e.g., communal behaviour) during pharmacological treatment as usual, namely during SSRI (i.e., paroxetine) administration.³⁴ Because SSRI medications are well established first-line treatments for adult social anxiety disorder, the present study examines whether improvements in affect and communal behaviour precede and predict later improvements in social anxiety symptom severity during community psychopharmacological treatment.

This study was conducted in Canada following the principles of the *Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans*,³⁵ which states that randomized clinical trials with 2 or more treatment groups can be conducted only when there is equipoise or genuine uncertainty among experts regarding the relative effectiveness of each treatment. Previous clinical trials have demonstrated the efficacy and effectiveness of paroxetine compared to placebo. Therefore, there is no equipoise between paroxetine and placebo treatment groups; the inclusion of a placebo group would have been inconsistent with the *Tri-Council Policy Statement*. Instead, paroxetine was administered in an open-label design with no placebo or control condition. In the present study, rather than evaluating the clinical effectiveness of SSRI medications, paroxetine administration facilitated an examination of whether changes in affective and behavioural correlates of social anxiety disorder mediated improvement in symptom severity.

Methods

Participants

Participants aged 20 to 60 years (mean \pm standard deviation 33.92 \pm 11.49) were recruited from the Montreal metropolitan area via community advertisements for a study of social anxiety disorder. Of participants who called to express interest, 48 provided informed consent and attended a baseline assessment, which included a description of the study and clinical assessment to establish the primary diagnosis of social anxiety disorder, baseline severity of social anxiety disorder, concurrent diagnoses and suitability for treatment with paroxetine (Paxil). Nine participants (18.75%) withdrew before paroxetine administration. The 39 participants (19 [48.7%] female) who began paroxetine administration approximated the educational distribution of Montreal, Quebec,³⁶ although psychiatric comorbidity was lower than expected.³⁷ Baseline assessment (see Measures) indicated severe symptoms of social anxiety disorder^{38,39} and mild depressive symptoms based on the Montgomery-Åsberg Depression Rating Scale.⁴⁰

Inclusion criteria, exclusion criteria and demographic details about the sample are provided in Rappaport and colleagues.³⁴ As reported in that paper, 31 participants (79.49%) completed baseline assessment and at least 3 months of treatment. Four (8.33%) discontinued treatment after 1 month; 4 (8.33%) discontinued after 2 months. Compared to participants who started paroxetine administration, withdrawal

before 3 months was not associated with age, sex, native language, education, employment, marital status or baseline severity of social anxiety disorder or depressive symptoms.

Design and procedure

This study followed an open-label, single-arm, nonrandomized, uncontrolled design that followed adults during the first 4 months of psychopharmacological treatment as usual for social anxiety disorder. Affect and communal behaviour were assessed using a measurement-burst design: participants completed 1 week of a standardized event-contingent recording procedure at baseline (i.e., before initiating paroxetine administration) and after 4, 8, 12 and 16 weeks of treatment. Following baseline assessment, to minimize potential adverse effects, study psychiatrists (G.P. and P.B.) supervised participants in initiating paroxetine controlled-release (Paxil CR) titrated from 12.5 mg/d to 25 mg/d according to each participant's response. Participants met with study psychiatrists monthly (i.e., at 4, 8, 12 and 16 weeks) to evaluate adverse effects and complete clinician- and participant-report assessments of the severity of social anxiety disorder symptoms. Participants provided informed consent before baseline assessment. This study was approved by the McGill University Research Ethics Board.

Event-contingent recording procedure

Participants reported on their affect (positive and negative), interpersonal behaviour (agreeable, quarrelsome, dominant, submissive) and perception of the behaviour of others with whom they interacted.²⁹ To minimize recall bias, participants completed a record immediately following substantial interpersonal interactions, defined as interactions lasting longer than 5 minutes.

Measures

Clinical assessment

Psychiatric diagnoses were evaluated using the semistructured Mini-International Neuropsychiatric Interview version 5,⁴¹ conducted by study psychiatrists. The severity of social anxiety and depressive symptoms were assessed dimensionally via clinician report on the Liebowitz Social Anxiety Scale (LSAS)⁴² and via participant report on the Social Interaction-Anxiety Scale (SIAS) and Social Phobia Scale (SPS).⁴³ On the LSAS, study psychiatrists rated participant fear/anxiety and avoidance of 24 social situations; on the SIAS and SPS, participants endorsed agreement with 20 items reflecting anxiety in social situations (e.g., "When mixing socially, I am uncomfortable"). Two items in the SIAS were reverse-coded. Previous research has demonstrated the reliability and validity of the LSAS, SIAS and SPS, including reliability at each time point for the present data.³⁴

Affect

Participants recorded event-level positive and negative affect based on 9 items balanced for affective intensity.⁴⁴ Items were averaged at each event to compute occasion-specific positive and negative affect. Positive and negative affect were then

averaged separately over events within each measurement wave (i.e., within each monthly 1-week assessment) to compute the average positive and average negative affect reported by each participant at each assessment wave. Previous research demonstrated reliability and validity in ecological momentary assessment and event-contingent recording procedures in similar community²⁹ and clinical samples,⁴⁵ including the present study.³⁴

Interpersonal behaviour

The present study conceptualized interpersonal behaviour according to the interpersonal circumplex model, which organizes the range of interpersonal behaviours on a biaxial system defined by orthogonal dimensions of communal (agreeable v. quarrelsome) and agentic (dominant v. submissive) behaviour. Participants reported their agreeable, quarrelsome, dominant and submissive behaviours at each event by reporting on representative behaviours using the Social Behaviour Inventory (SBI; e.g., "I showed sympathy").^{29,46} Items representing each of the 4 poles were summed and ipsatized at each event to adjust for each participant's general endorsement tendency.⁴⁷ Similar to affect, agreeable behaviour and quarrelsome behaviour were averaged separately over events within each measurement wave to compute the average agreeable and quarrelsome behaviour reported by each participant at each assessment wave. Agreeable and quarrelsome behaviour assessments were then multiplied by 10 to enable computational modelling. Within an event-contingent recording procedure, the SBI has demonstrated strong psychometric properties,²⁹ including agreement with observer report of participant behaviour,⁴⁸ suitability for use in clinical samples⁴⁹ and sensitivity to change during pharmacological intervention.^{12,34}

Data analysis

Data analysis followed 3 steps to build bivariate latent change score models, which evaluate time-lagged associations of affect and communal behaviour with later change in social anxiety severity.^{24,25} First, we developed a measurement model for social anxiety symptom severity and extracted latent social anxiety severity from a factor model as indicated by monthly clinician- and participant-report assessments (see Appendix 1, Table S1, available at jpn.ca/190164-a1). Second, we fit separate latent change score models to each construct (e.g., mean positive affect) to examine change in social anxiety severity, agreeable and quarrelsome behaviour, and positive and negative affect over time. Each latent change score model followed the dual-change score framework to partition linear change over time from proportional change over each month of pharmacological treatment.²⁵ Within each latent change score model, we found no statistical evidence of phi (ϕ ; p values > 0.10), which assesses whether early change in each process (e.g., from baseline to month 1) predicts the magnitude of later change (e.g., from month 1 to month 2). Subsequent analyses were conducted without ϕ paths.

Finally, in separate models, we combined the latent change score model describing change in social anxiety severity with that describing change in agreeable behaviour, quarrelsome

behaviour, positive affect and negative affect. Thus, following the approach developed by Grimm and colleagues,²⁴ 4 bivariate latent change score models evaluated time-lagged associations of affect and communal behaviour with previous and subsequent change in social anxiety severity. The resulting bivariate latent change score models examined whether the level of each affective or interpersonal process (e.g., mean positive affect) predicted subsequent change in social anxiety severity. These models simultaneously examined whether the change in each process predicted subsequent change in social anxiety severity. In both cases, the bivariate latent change score model adjusted for linear and nonlinear change across time. Importantly, the bivariate latent change score model represented both variables together and allowed for reciprocal influence. Thus, the bivariate latent change score models also examined and adjusted for the alternative possibility that the level of, or change in, social anxiety severity may predict subsequent change in each process (e.g., mean positive affect).

Given the large number of bivariate latent change score models under consideration, the present study limited examination to affect and communal (i.e., agreeable and quarrelsome) behaviour, which extant evidence implicates in the pharmacological treatment of social anxiety disorder.^{10,21} Relative to change from baseline to 12 weeks, there was little additional change in affect, communal behaviour or social anxiety severity from 12 to 16 weeks of treatment.³⁴ Therefore, to examine temporal patterns of change, the present study analyzed only data collected before the final assessment in week 16.

Analyses were conducted in R version 3.5.2⁵⁰ using the ggplot2⁵¹ and OpenMx packages.⁵² Structural equation modelling estimation used full information maximum likelihood, which is robust to data missing at, or conditionally at, random.⁵³ Because of model complexity, confidence intervals (CIs) were estimated using bootstrapping.

Ethical standards

The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008.

Results

Change in affect, communal behaviour and social anxiety symptom severity

Over time, participants demonstrated increased mean positive affect and agreeable behaviour, along with decreased mean negative affect, quarrelsome behaviour and social anxiety symptom severity (see Table 1 for descriptive data, and Table 2 and Fig. 1 for change described by each latent change score model). Improvements in symptom severity, affect and interpersonal behaviour were consistent with previous evidence from multilevel, mixed-effects growth curve and location-scale analyses.³⁴ Including latent social anxiety severity, all 5 individual latent change models indicated good or adequate fit to the data (Table 2). For all 4 models of affect and communal behaviour, strict measurement invariance was confirmed by nonsignificant increases in the log-likelihood when constraining all residual variances to be equal across time ($p > 0.13$); see Appendix 1 for information on time invariance of social anxiety severity). Parameter estimates (Table 2) and expected means (Fig. 1) represented each latent change score model of best fit (i.e., with no ϕ paths and time invariant residual variances).

Association of change in affect and communal behaviour with change in social anxiety symptom severity

Having clarified the models of best fit for change in affect, communal behaviour and social anxiety severity, we used bivariate latent change score models to examine time-lagged associations of change in social anxiety severity with levels of and change in positive affect, negative affect, agreeable behaviour and quarrelsome behaviour (Fig. 2). All 4 models fit the data well or adequately (Table 3). Three of the 4 models indicated that improvements in affect and agreeable behaviour preceded and predicted subsequent improvements in social anxiety severity. Higher levels of positive affect ($B = -1.41$, 95% CI -3.84 to -0.31 ; $p = 0.009$) and agreeable behaviour ($B = -2.16$, 95% CI -7.66 to -0.29 ; $p = 0.001$) predicted greater subsequent reduction in social anxiety severity over each following month. Similarly, higher levels of negative affect ($B = 1.31$, 95% CI 0.45 to 3.87 ; $p < 0.001$), but not

Table 1: Descriptive statistics at each assessment wave

Measure	Baseline*	Time 1*	Time 2*	Time 3*
Liebowitz Social Anxiety Scale	85.96 ± 19.03	60.79 ± 28.92	47.11 ± 24.77	44.83 ± 27.22
Social Phobia Scale	45.74 ± 14.26	34.08 ± 15.78	25.11 ± 15.76	22.81 ± 16.28
Social Interaction–Anxiety Scale	54.64 ± 9.56	41.90 ± 14.54	33.16 ± 15.48	31.47 ± 16.56
Positive affect†	2.17 ± 1.04	2.55 ± 1.17	2.85 ± 1.23	2.83 ± 1.34
Negative affect†	1.34 ± 0.75	0.84 ± 0.70	0.59 ± 0.55	0.48 ± 0.50
Agreeable behaviour†	1.05 ± 0.96	1.65 ± 0.95	1.81 ± 1.14	1.80 ± 1.19
Quarrelsome behaviour†	-1.43 ± 0.86	-1.69 ± 0.89	-1.63 ± 0.91	-1.79 ± 0.70

*All values are mean ± standard deviation. Time 1 indicates 4 weeks after treatment initiation; time 2 indicates 8 weeks after treatment initiation; time 3 indicates 12 weeks after treatment initiation.

†Mean of event-contingent recording reports within each assessment wave (i.e., each monthly 1-week assessment) for each participant; behaviour assessments were multiplied by 10 to enable computational models.

Table 2: Parameter estimation and model fit for “univariate” latent change score models of anxiety symptom severity, affect and communal behaviour

Measure	Social anxiety	Positive affect	Negative affect	Agreeable behaviour	Quarrelsome behaviour
Parameter, B (95% CI)					
β^*	-0.56 (-0.68 to -0.44)‡	-0.49 (-0.80 to -0.11)§	-0.49 (-0.66 to -0.29)‡	-0.77 (-1.06 to -0.42)‡	-0.79 (-1.27 to -0.24)§
M_{int}	5.81 (5.62 to 5.99)‡	2.18 (1.88 to 2.48)‡	1.33 (1.11 to 1.55)‡	1.05 (0.78 to 1.33)‡	-1.44 (-1.69 to -1.20)‡
s^2_{int}	0.43 (0.38 to 0.90)¶	0.85 (0.77 to 1.42)‡	0.52 (0.34 to 0.84)‡	0.50 (0.19 to 0.99)¶	0.52 (0.27 to 0.92)‡
M_{slope}	2.26 (1.63 to 2.92)‡	1.50 (0.52 to 2.34)¶	0.19 (-0.02 to 0.40)	1.42 (0.88 to 1.95)‡	-1.36 (-2.20 to -0.47)¶
s^2_{slope}	0.36 (0.32 to 0.63)‡	0.36 (0.32 to 0.95)¶	0.08 (0.03 to 0.16)‡	0.49 (0.44 to 1.04)‡	0.37 (0.33 to 0.97)‡
Covariance (int. with slope)	0.08 (-0.06 to 0.25)	0.47 (0.12 to 0.95)§	0.06 (-0.05 to 0.18)	0.27 (0.03 to 0.63)§	0.26 (0.03 to 0.62)§
e^{\ddagger}	—	0.23 (0.16 to 0.32)	0.08 (0.06 to 0.11)	0.40 (0.29 to 0.57)	0.22 (0.16 to 0.32)
Model fit					
χ^2	$\chi^2_{4} = 2.49$ $p = 0.64$	$\chi^2_{7} = 6.99$ $p = 0.43$	$\chi^2_{7} = 14.86$ $p = 0.04$	$\chi^2_{7} = 4.74$ $p = 0.69$	$\chi^2_{7} = 10.03$ $p = 0.19$
CFI	1.01	1.00	0.90	1.05	0.95
RMSEA (95% CI)	0 (0 to 0.20)	0 (0 to 0.20)	0.15 (0 to 0.28)	0 (0 to 0.16)	0.09 (0 to 0.23)

CFI = comparative fit index; CI = confidence interval; Covariance (int. with slope) = covariance of the mean intercept (baseline severity) with the mean slope describing the average linear change over time; e^{\ddagger} = error variances; M_{int} = the mean intercept (baseline severity); M_{slope} = the mean slope describing linear change over time; RMSEA = root mean square error of approximation; s^2_{int} = between-person variance of the intercept; s^2_{slope} = between-person variance of the slope describing linear change over time.

*Similar to multilevel models or latent growth curve models in other structural equation modeling approaches, β represents the regression of change over each month on prior level.

‡Significance tests were not conducted for error variances; see Data Analysis for information on the time invariance of anxiety symptom severity.

‡ $p < 0.001$.

§ $p < 0.05$.

¶ $p < 0.01$.

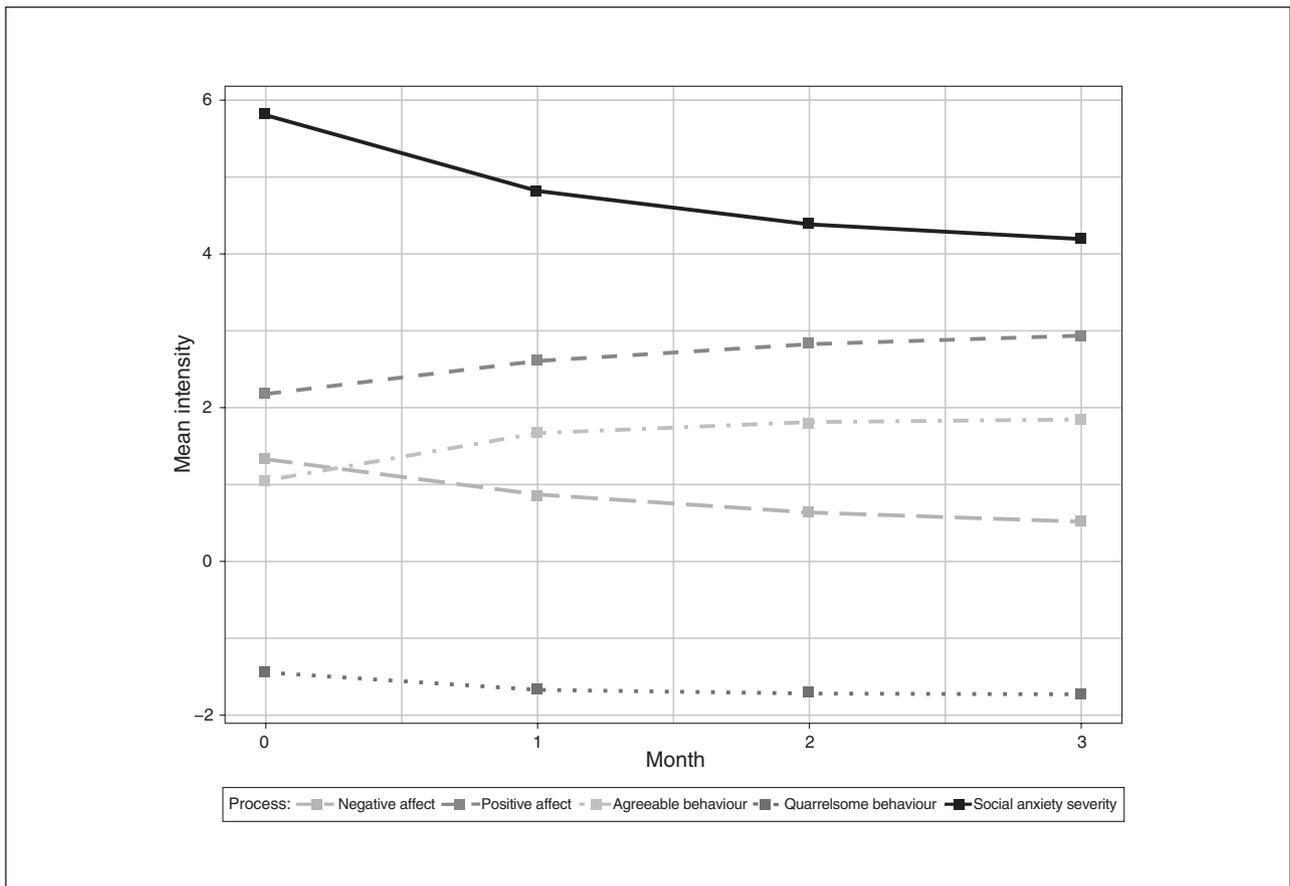


Fig. 1: Expected means for latent social anxiety severity, negative affect, positive affect, agreeable behaviour and quarrelsome behaviour over time.

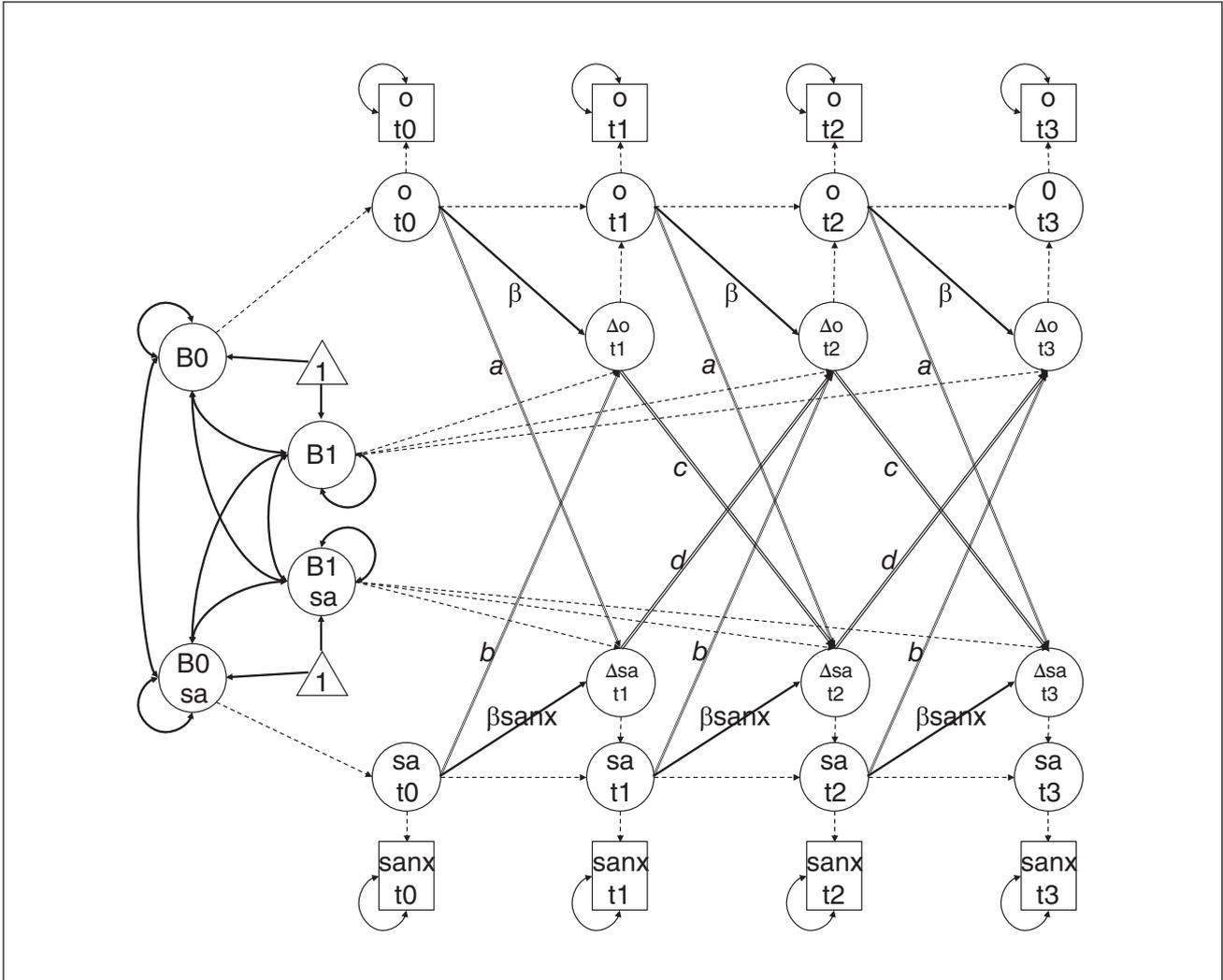


Fig. 2: Example of a bivariate latent change score model. This model was run 4 separate times to examine the association of change in social anxiety severity with change in positive affect, negative affect, agreeable behaviour and quarrelsome behaviour, which were entered in the observed variables o_{t0} , o_{t1} , o_{t2} and o_{t3} . Solid lines indicate estimated paths; dotted lines indicate paths fixed at 1; a indicates time-invariant regression of change in social anxiety severity on prior level of the psychological process; b indicates time-invariant regression of change in the psychological process on prior level of social anxiety severity; c indicates regression of change in social anxiety severity on prior change in the psychological process; d indicates regression of change in the psychological process on prior change in social anxiety severity. A time-invariant covariance was estimated between concurrent measures of the psychological process and social anxiety severity (e.g., o_{it} with a_{it}). Δ = change; $B0$ = intercept for the psychological process modelled; $B1$ = linear slope for the psychological process modelled; $B0sa$ = intercept for social anxiety severity; $B1sa$ = linear slope for social anxiety severity; o = one of the 4 psychological processes (e.g., positive affect); sa = the factor score for latent social anxiety severity (see Data Analysis); $sanx$ = social anxiety; $t0$ = baseline; $t1$ = 4 weeks after treatment initiation; $t2$ = 8 weeks after treatment initiation; $t3$ = 12 weeks after treatment initiation.

Table 3: Model fit for “bivariate” latent change score models of affect and communal behaviour with social anxiety symptom severity

Measure	Positive affect	Negative affect	Agreeable behaviour	Quarrelsome behaviour
χ^2	$\chi^2_{21} = 22.95$ $p = 0.35$	$\chi^2_{21} = 21.07$ $p = 0.45$	$\chi^2_{21} = 29.67$ $p = 0.10$	$\chi^2_{21} = 34.59$ $p = 0.03$
CFI	0.99	1.00	0.95	0.92
RMSEA (95% CI)	0.04 (0 to 0.15)	0.01 (0 to 0.14)	0.09 (0 to 0.18)	0.12 (0 to 0.19)

CFI = comparative fit index; CI = confidence interval; RMSEA = root mean square error of approximation.

quarrelsome behaviour ($B = 3.70$, 95% CI -3.38 to 14.57 ; $p = 0.18$), predicted less subsequent reduction in social anxiety severity over each following month.

Despite limited power, we found no evidence that level of or change in social anxiety symptom severity predicted subsequent change in positive affect or communal behaviour ($p > 0.35$). Notwithstanding possible α inflation due to multiple testing, higher levels of social anxiety severity — but not change in social anxiety severity ($p = 0.11$) — may predict greater subsequent reduction in negative affect ($B = -0.23$, 95% CI -0.90 to 0.08 ; $p = 0.03$). Similarly, we found no evidence that change in affect or communal behaviour predicted subsequent change in social anxiety severity ($p > 0.23$). After adjusting for temporally lagged associations, we found no evidence of concurrent correlations of social anxiety symptom severity with affect or communal behaviour at baseline ($p > 0.06$) or of correlated linear change over the course of treatment ($p > 0.09$).

Discussion

The present study documents increased positive affect and agreeable behaviour, along with decreased negative affect and quarrelsome behaviour, in the daily lives of adults receiving SSRI treatment (i.e., paroxetine) for social anxiety disorder. Moreover, in 3 of 4 models tested, improvements in affect and agreeable behaviour preceded and predicted greater subsequent reduction of social anxiety symptom severity as reported by participants and their treating psychiatrists.

Evidence that improved agreeable behaviour predicts subsequent clinical improvement is consistent with the Social Interaction Model. For example, extant evidence also demonstrates that serotonin modulation via administration of tryptophan¹² or SSRI medication¹⁸ increases prosocial behaviour^{14–16} and reduces behavioural variability,⁵⁴ including in the present study.³⁴ Similarly, evidence that increased positive and decreased negative affect predicts subsequent clinical improvement is consistent with the Cognitive Neuropsychological Model. For example, extant evidence also demonstrates that among healthy volunteers⁵⁵ and individuals with a depressive disorder,⁵⁶ administration of serotonergic medications may increase face emotion recognition, which is also implicated in the etiology of neuroticism and depressive disorders.^{57,58} Emerging research further indicates potential neural correlates of SSRI administration, which may reflect normalization of aberrant pretreatment activity.⁵⁹ The present results provide an important extension of previous research to demonstrate that, during standard psychopharmacological treatment, improvements in affect and communal behaviour precede and predict subsequent clinical improvement in social anxiety severity as assessed by both the patient and the clinician.

By assessing affect and communal behaviour naturalistically in an event-contingent recording design, improvements in affect and communal behaviour represented changes manifested in participants' daily lives. Increased agreeable and decreased quarrelsome behaviour may facilitate positive social encounters by disrupting a cycle of interpersonal problems that may maintain social anxiety disorder.⁶⁰ By demonstrating

putative psychological targets for pharmacological treatment as usual of social anxiety disorder, the present data encourage further research into the psychobiological mechanisms underlying pharmacological and psychological interventions.

Limitations

The present results warrant consideration in light of several limitations, which should be addressed in future research. The SBI assesses the range of behaviours typical in interpersonal interactions of community adults.⁴⁶ Although it has been well validated in community²⁹ and clinical samples,⁴⁵ including among individuals with social anxiety disorder,⁴⁹ the SBI does not include rarer, clinically relevant behaviours. For example, given evidence implicating serotonergic dysregulation in aggression,²⁰ future research is needed to examine changes in interpersonal aggression that is more severe than quarrelsome behaviour.

The present study also provides an initial examination into whether affective and interpersonal changes precede or follow from improvements in social anxiety symptom severity. Given the relatively small sample size, evident statistically significant results in 3 of 4 models illustrate the strength of the associations documented here. Future research with a larger sample is necessary to fully rule out an alternative explanation that social anxiety severity may also predict latter change in affect or communal behaviour.

Finally, consideration of ethical research practice — specifically the principle of equipoise — prevented the inclusion of a placebo control group, randomization and clinical blinding. Future research is needed to evaluate alternative explanations, such as the beneficial impact of clinical attention or reflecting on one's affect and interpersonal behaviour. However, previous research with community adults demonstrates that mean affect and interpersonal behaviour are highly stable over multiple weeks.^{29,46} High stability over time suggests that the event-contingent recording procedure may not substantially bias participant report.

Conclusion

The present study extends previous evidence of increased prosocial behaviour, increased positive affect and reduced negative affect following serotonin modulation with SSRI medication. Specifically, the present study demonstrates that during treatment as usual with paroxetine, improvements in affect and agreeable behaviour in participants' daily lives temporally precede and predict subsequent reduction in social anxiety symptom severity. Although it is preliminary, evidence that affective and interpersonal changes mediate clinical improvement during pharmacological treatment as usual encourages further research to examine affect and interpersonal behaviour as putative mechanisms of action to partially explain and refine the treatment of social anxiety disorder.

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Funding: The research was partially supported by a grant from the National Institute of Mental Health (T32MH020030) and a grant from GlaxoSmithKline, who was not authorized to review the findings or manuscript, or to comment on publication as per the policy of McGill University.

Data sharing: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Competing interests: None declared.

Contributors: J. Russell, G. Pinard, P. Bleau and D. Moskowitz initially designed the study and acquired the data. L. Rappaport designed the present study as a secondary analysis of previously collected data and conducted planned analyses with M. Hunter. L. Rappaport, M. Hunter and D. Moskowitz wrote the article, which all authors reviewed. All authors approved the final version to be published and can certify that no other individuals not listed as authors have made substantial contributions to the paper.

References

- American Psychiatric Association. *Diagnostic and statistical manual of mental disorders*. 5th ed. Washington (DC): APA; 2013.
- Alden LE, Bieling P. Interpersonal consequences of the pursuit of safety. *Behav Res Ther* 1998;36:53-64.
- Schmidt NB, Short N, Stanley I, et al. Anxiety sensitivity. In: Olatunji BO, editor. *The Cambridge handbook of anxiety and related disorders*. Cambridge: Cambridge University Press; 2019:121-62.
- Strong SR, Hills H, Kilmartin CT, et al. The dynamic relations among interpersonal behaviors: a test of complementarity and anticomplementarity. *J Pers Soc Psychol* 1988;54:798-810.
- Fedoroff IC, Taylor S. Psychological and pharmacological treatments of social phobia: a meta-analysis. *J Clin Psychopharmacol* 2001;21:311-24.
- Stein MB, Liebowitz MR, Lydiard RB, et al. Paroxetine treatment of generalized social phobia (social anxiety disorder): a randomized controlled trial. *JAMA* 1998;280:708-13.
- Katzman MA, Bleau P, Blier P, et al; the Canadian Anxiety Guidelines Initiative Group on behalf of the Anxiety Disorders Association of Canada/Association Canadienne des troubles anxieux and McGill University. Canadian clinical practice guidelines for the management of anxiety, posttraumatic stress and obsessive-compulsive disorders. *BMC Psychiatry* 2014;14(Suppl 1):S1.
- Canadian Psychiatric Association. Clinical practice guidelines: management of anxiety disorders. *Can J Psychiatry* 2006;51:9S-91S.
- Harmer CJ, Duman RS, Cowen PJ. How do antidepressants work? New perspectives for refining future treatment approaches. *Lancet Psychiatry* 2017;4:409-18.
- Harmer CJ. Emotional processing and antidepressant action. In: Cowen P, Sharp T, Lau J, editors. *Behavioral neurobiology of depression and its treatment: current topics in behavioral neurosciences*. Berlin: Springer; 2012.
- Raleigh MJ, McGuire MT. Bidirectional relationships between tryptophan and social behavior in vervet monkeys. *Adv Exp Med Biol* 1991;294:289-98.
- Moskowitz DS, Pinard G, Zuroff DC, et al. The effect of tryptophan on social interaction in everyday life: a placebo-controlled study. *Neuropsychopharmacology* 2001;25:277-89.
- Young SN. Behavioral effects of dietary neurotransmitter precursors: basic and clinical aspects. *Neurosci Biobehav Rev* 1996;20:313-23.
- Tse WS, Bond A. Serotonergic intervention affects both social dominance and affiliative behaviour. *Psychopharmacology (Berl)* 2002;161:324-30.
- Tse WS, Bond AJ. Difference in serotonergic and noradrenergic regulation of human social behaviours. *Psychopharmacology (Berl)* 2002;159:216-21.
- Tse WS, Bond AJ. Reboxetine promotes social bonding in healthy volunteers. *J Psychopharmacol* 2003;17:189-95.
- Aan het Rot M, Moskowitz DS, Pinard G, et al. Social behaviour and mood in everyday life: the effects of tryptophan in quarrelsome individuals. *J Psychiatry Neurosci* 2006;31:253-62.
- Knutson B, Wolkowitz OM, Cole SW, et al. Selective alteration of personality and social behavior by serotonergic intervention. *Am J Psychiatry* 1998;155:373-9.
- Raleigh MJ, McGuire MT, Brammer GL, et al. Serotonergic mechanisms promote dominance acquisition in adult male vervet monkeys. *Brain Res* 1991;559:181-90.
- Bjork JM, Dougherty DM, Moeller FG, et al. The effects of tryptophan depletion and loading on laboratory aggression in men: time course and a food-restricted control. *Psychopharmacology (Berl)* 1999;142:24-30.
- Young SN, Moskowitz DS, aan het Rot M. Possible role of more positive social behaviour in the clinical effect of antidepressant drugs. *J Psychiatry Neurosci* 2014;39:60-5.
- Harmer CJ, Cowen PJ. 'It's the way that you look at it' — a cognitive neuropsychological account of SSRI action in depression. *Philos Trans R Soc Lond B Biol Sci* 2013;368:20120407.
- Harmer CJ, Goodwin GM, Cowen PJ. Why do antidepressants take so long to work? A cognitive neuropsychological model of antidepressant drug action. *Br J Psychiatry* 2009;195:102-8.
- Grimm KJ, An Y, McArdle JJ, et al. Recent changes leading to subsequent changes: extensions of multivariate latent difference score models. *Struct Equ Modeling* 2012;19:268-92.
- McArdle JJ. Latent variable modeling of differences and changes with longitudinal data. *Annu Rev Psychol* 2009;60:577-605.
- Hawley LL, Ho M-HR, Zuroff DC, et al. The relationship of perfectionism, depression, and therapeutic alliance during treatment for depression: latent difference score analysis. *J Consult Clin Psychol* 2006;74:930-42.
- Shiffman S, Stone AA, Hufford MR. Ecological momentary assessment. *Annu Rev Clin Psychol* 2008;4:1-32.
- Houben M, Van Den Noortgate W, Kuppens P. The relation between short-term emotion dynamics and psychological well-being: a meta-analysis. *Psychol Bull* 2015;141:901-30.
- Moskowitz DS, Sadikaj G. Event-contingent sampling. In: Mehl T, Conner T, editors. *Handbook of research methods for studying daily life*. New York: Guilford Press; 2011:160-75.
- Côté S, Moskowitz DS, Zuroff DC. Social relationships and intraindividual variability in interpersonal behavior: correlates of interpersonal spin. *J Pers Soc Psychol* 2012;102:646-59.
- Sadikaj G, Rappaport LM, Moskowitz DS, et al. Consequences of interpersonal spin on couple-relevant goal progress and relationship satisfaction in romantic relationships. *J Pers Soc Psychol* 2015;109:722-37.
- Eid M, Diener E. Intraindividual variability in affect: reliability, validity, and personality correlates. *J Pers Soc Psychol* 1999;76:662-76.
- Mogg K, Mathews A, Weinman J. Memory bias in clinical anxiety. *J Abnorm Psychol* 1987;96:94-8.
- Rappaport LM, Russell JJ, Hedeker D, et al. Affect, interpersonal behaviour and interpersonal perception during open-label, uncontrolled paroxetine treatment of people with social anxiety disorder: a pilot study. *J Psychiatry Neurosci* 2018;43:407-15.
- Canadian Institutes of Health Research, Natural Sciences and Engineering Research Council of Canada, and Social Sciences and Humanities Council of Canada. *Tri-Council policy statement: ethical conduct for research involving humans*. Ottawa (ON): Secretariat on Responsible Conduct of Research; 2018.
- Distribution of the population aged 25 to 64 by highest level of education attained, Montréal and all of Québec, 2011–2015 (table)*. Québec: Institut de la statistique du Québec; 2017. Available: http://www.stat.gouv.qc.ca/statistiques/profils/profil06/societe/education/niveau_scolaire06_an.htm (accessed 2020 Jun 25).
- Kessler RC, Berglund P, Demler O, et al. Lifetime prevalence and age-of-onset distributions of DSM-IV disorders in the National Comorbidity Survey Replication. *Arch Gen Psychiatry* 2005;62:593-602.
- Brown EJ, Turovsky J, Heimberg RG, et al. Validation of the Social Interaction Anxiety Scale and the Social Phobia Scale across the anxiety disorders. *Psychol Assess* 1997;9:21.
- Mennin DS, Fresco DM, Heimberg RG, et al. Screening for social anxiety disorder in the clinical setting: using the Liebowitz Social Anxiety Scale. *J Anxiety Disord* 2002;16:661-73.
- Mittmann N, Mitter S, Borden EK, et al. Montgomery-Asberg severity gradations. *Am J Psychiatry* 1997;154:1320-1.

41. Sheehan DV, Lecrubier Y, Sheehan KH, et al. The Mini International Neuropsychiatric Interview (MINI): the development and validation of a structured diagnostic psychiatric interview for DSM-IV and ICD-10. *J Clin Psychiatry* 1998;59:22-33.
42. Liebowitz MR. Update on the diagnosis and treatment of social anxiety disorder. *J Clin Psychiatry* 1999;60(Suppl 18):22-6.
43. Mattick RP, Clarke JC. Development and validation of measures of social phobia scrutiny fear and social interaction anxiety. *Behav Res Ther* 1998;36:455-70.
44. Diener E, Emmons RA. The independence of positive and negative affect. *J Pers Soc Psychol* 1984;47:1105-17.
45. Russell JJ, Moskowitz DS, Zuroff DC, et al. Stability and variability of affective experience and interpersonal behavior in borderline personality disorder. *J Abnorm Psychol* 2007;116:578-88.
46. Moskowitz DS. Cross-situational generality and the interpersonal circumplex. *J Pers Soc Psychol* 1994;66:921-33.
47. Horowitz LM, Rosenberg SE, Baer BA, et al. Inventory of interpersonal problems: psychometric properties and clinical applications. *J Consult Clin Psychol* 1988;56:885-92.
48. Mongrain M, Vettese LC, Shuster B, et al. Perceptual biases, affect, and behavior in the relationships of dependents and self-critics. *J Pers Soc Psychol* 1998;75:230-41.
49. Russell JJ, Moskowitz DS, Zuroff DC, et al. Anxiety, emotional security and the interpersonal behavior of individuals with social anxiety disorder. *Psychol Med* 2011;41:545-54.
50. R Core Team. R: *A Language and Environment for Statistical Computing*. Vienna: R Foundation for Statistical Computing; 2018. Available: <https://www.R-project.org/> (accessed 2020 Jun 25).
51. Wickham H. *ggplot2: elegant graphics for data analysis*. New York: Springer-Verlag; 2009.
52. Neale MC, Hunter MD, Pritikin JN, et al. OpenMx 2.0: extended structural equation and statistical modeling. *Psychometrika* 2016; 81:535-49.
53. Little TD, Jorgensen TD, Lang KM, et al. On the joys of missing data. *J Pediatr Psychol* 2014;39:151-62.
54. Moskowitz DS, Zuroff DC, aan het Rot M, et al. Tryptophan and interpersonal spin. *J Res Pers* 2011;45:692-6.
55. Harmer CJ, Bhagwagar Z, Perrett DI, et al. Acute SSRI administration affects the processing of social cues in healthy volunteers. *Neuropsychopharmacology* 2003;28:148-52.
56. Tranter R, Bell D, Gutting P, et al. The effect of serotonergic and noradrenergic antidepressants on face emotion processing in depressed patients. *J Affect Disord* 2009;118:87-93.
57. Dalili MN, Penton-Voak IS, Harmer CJ, et al. Meta-analysis of emotion recognition deficits in major depressive disorder. *Psychol Med* 2015;45:1135-44.
58. Rappaport LM, Carney DM, Verhulst B, et al. A developmental twin study of emotion recognition and its negative affective clinical correlates. *J Am Acad Child Adolesc Psychiatry* 2018;57: 925-33.e3.
59. Furmark T, Tillfors M, Marteinsdottir I, et al. Common changes in cerebral blood flow in patients with social phobia treated with citalopram or cognitive-behavioral therapy. *Arch Gen Psychiatry* 2002; 59:425-33.
60. Alden LE, Taylor CT. Interpersonal processes in social phobia. *Clin Psychol Rev* 2004;24:857-82.