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Research report

The Oxford Questionnaire on the Emotional Side-effects of Antidepressants (OQuESA): Development, validity, reliability and sensitivity to change

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ABSTRACT

Background: Some patients with major depression report a restricted range of emotions that may appear to arise as a side-effect of treatment with antidepressants. It is uncertain whether this phenomenon, sometimes called emotional blunting, represents residual symptoms of depression or side-effects of antidepressant treatment. There is currently no adequate instrument to measure this phenomenon.
Methods: A draft questionnaire was developed from patient-derived qualitative data, refined using cognitive interviewing, and administered on three occasions to patients taking antidepressants. Statistical methods including factor analysis were used to reduce the size of the draft questionnaire, and to assess the performance of the resulting Oxford Questionnaire on the Emotional Side-effects of Antidepressants (OQuESA).
Results: 207 patients completed the OQuESA on at least one occasion. Their BDI-II scores and self-reported emotional blunting were spread across the possible range. The factor analysis resulted in four dimensions: 'not caring', 'emotional detachment', 'reduction in positive emotions', and 'general reduction in emotions'. The OQuESA appears to be acceptable, valid, and reliable, with sensitivity to change.
Conclusions: The OQuESA offers promise as an effective self-report measure of the symptoms of emotional blunting in patients with depression. It can be used as a clinical tool, to facilitate the identification of patients with the syndrome of emotional blunting. It should also be used in research studies, to advance our understanding of the nature, causes and treatment of this phenomenon.

1. Introduction

Some patients with major depression report subjective symptoms that may appear to arise as a side-effect of treatment with antidepressants. Some are well known and well characterised, such as anxiety and agitation. Other symptoms are more subtle and elude measurement by conventional scales for depression. Thus, patients report that, while they feel less emotional pain than before commencing their antidepressant, they also experience a restricted range of emotions and, in particular, cannot get a "normal" emotional response to everyday events that would usually be associated with, for example, joy or sadness. It is uncertain whether this phenomenon, sometimes called 'emotional blunting', represents residual symptoms of depression or side-effects of antidepressant treatment.

It is now well established that antidepressants can modify the processing of emotional material (Harmer et al., 2009a). A behavioural effect is seen after a single dose in healthy volunteers, and after a week, antidepressants modify unconscious processing of negative facial expression (Harmer et al., 2006). In patients, negative biases in acutely depressed

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patients and in recovered patients are attenuated by short term treatment with antidepressants (Bhagwagar et al., 2004; Harmer et al., 2009b). A reduced sensitivity to negative emotional stimuli might result from these effects of antidepressants and be expressed as emotional blunting. In healthy volunteers taking antidepressants, emotional blunting seems not to be reported, and in patients the presence of emotional blunting is difficult to distinguish from the expected symptoms of depression. However, for neither group have we necessarily had the right instrument to measure this experience.

The two existing instruments which claim to measure emotional blunting in this context appear to lack either careful design or validation. The first is the Laukes Emotional Intensity Scale (LEIS; no primary citation available, but described in Opbroek et al., 2002), a self-report instrument comprising 18 questions asking patients to rate an aspect of their emotional life compared to their 'usual' state along a 5 point scale (a lot less/somewhat less/same as usual/somewhat more/a lot more). A group of patients taking SSRIs and reporting sexual side-effects reported significant reductions in 12 of the 18 items, including ability to cry, irritation, care about others' feelings, sadness, erotic dreaming, creativity, surprise, anger, expression of their feelings, worry, sexual pleasure, and interest in sex (Opbroek et al., 2002). The second is the Bell–Shipman apathy/emotional blunting questionnaire (BSAQ; Bell et al., 2006), which comprises 5 self-completion questions. It is described in the study report as 'under development', but there are no published details of its completion.

The aims of the present study were: a) to create a draft version of a questionnaire that would comprehensively capture the experience of emotional blunting, derived from careful interviewing of patients taking antidepressants; b) to refine this draft questionnaire, by removing redundant and less effective items, thereby creating the final questionnaire; and c) to evaluate the performance of the final questionnaire, including acceptability, construct validity, internal consistency reliability, split-half reliability, test–retest reliability, and sensitivity to change.

2. Method

2.1. Part 1: creation of a draft questionnaire

Because of the apparent complexity of emotional blunting, and its probable overlap with some symptoms of depression, careful qualitative work was undertaken, and is described elsewhere (Price et al., 2009). A comprehensive bank of possible questionnaire items was created from the qualitative dataset. Eleven of the original 38 participants in the qualitative study were re-interviewed to a) validate the qualitative findings and b) refine possible questionnaire items through field testing and cognitive interviewing. A draft questionnaire of emotional side-effects of antidepressants, suitable for subsequent quantitative evaluation, was created. This draft questionnaire incorporated neither items derived from other measures nor items derived by asking clinicians, as the intention was to develop a measure derived directly from patient experiences of emotional side-effects.

2.2. Part 2: refinement of the draft questionnaire

2.2.1. Participants

Ethical approval for this research was obtained from Oxfordshire Research Ethics Committee C (study number 07/H0606/117). Inclusion criteria for study participation were: a) age over 18 years; b) resident in the United Kingdom; c) fluent in spoken/written English; and d) taking an antidepressant regularly, for any reason. 'Antidepressant' was defined as any medicine listed in Section 4.3 of the British National Formulary version 53 (Joint Formulary Committee, 2007). We recruited participants a) via Oxfordshire GPs and psychiatrists; b) by direct approach from us to participants in a previous study (Price et al., 2009); c) by poster in, for example, general practice waiting areas and public libraries; d) by advertisement in a local information sheet; and e) by promotion on websites. We screened potential participants by phone or email to confirm eligibility.

2.2.2. Data gathering

Data were gathered at week 0, week 1 and week 4. At week 0, we gathered background data on participants, including details of antidepressant use (drug name, current dose, duration of intake, and adherence), and names of other medicines taken regularly, including St John's Wort; the Beck Depression Inventory — II (BDI-II; Beck et al., 1996); the draft questionnaire; and response to a 'gold standard' question relating to the participant's experience of emotional side-effects. At week 1 and week 4, we repeated questions relating to current medication, the gold standard question, and the draft questionnaire.

The 'gold standard' question asked participants to respond 'not at all', 'insignificantly', 'mildly', 'moderately' or 'severely' to the question 'During the last week, to what extent have you been experiencing emotional side-effects of your antidepressant?' The question's subscript reads 'Emotional side-effects are varied, but might include, for example — feeling emotionally 'numbed' or 'blunted' in some way/lacking positive emotions or negative emotions/feeling detached from the world around you/'just not caring' about things that you used to care about.' We considered carefully whether to use one of the two existing instruments (the LEIS or the BSAQ) as the gold standard performance comparison for the OQuESA. However, neither instrument has published details regarding its design or validation, and it is therefore not clear how or to what extent they measure a coherent phenomenon. We therefore preferred to use a single pragmatic question, designed by careful reference to data derived from extensive interviews of people with self-reported emotional blunting (Price et al., 2009), which we believed would effectively signify to participants the experience that we were intending to capture.

Our preferred method of data gathering was online, via a secure website at https://www.smart-survey.co.uk/. Not every participant was willing or able to complete questionnaires online, and so we also offered data gathering by paper questionnaires.

2.2.3. Data analysis

We analysed data from Section 3 of the questionnaire 7(beliefs about side-effects of antidepressants) separately

from data from Sections 1 and 2 (items addressing emotional side-effects). For each item, we determined the frequency distribution of the percentage of respondents for each response category, and calculated the median and interquartile range of the individual mean scores. We determined key performance characteristics for each questionnaire item by a) identifying items with significant ceiling or floor effects, b) cross-tabulating responses with those to the gold-standard question to generate both the kappa statistic and associated probability, and Kendall's tau-b statistic and associated probability, and c) calculating the corrected item–total correlation. We used these characteristics to guide the exclusion of some items prior to undertaking factor analysis.

We conducted a series of factor analyses, adopting an iterative approach to the exclusion of questionnaire items, according to the results of the previous factor analysis. In each round, surviving items were fed into a further factor analysis, which informed the exclusion of further items, until a consistent factor solution was generated. We used principal components factor analysis, with varimax rotation, and included factors with eigenvalues (representing the amount of variance accounted for by each factor) greater than 1. Individual items with loadings of less than 0.5 to a factor were excluded from the next factor analysis, as were items clearly cross-loading to more than one factor. We analysed data from Section 3 similarly to that from Sections 1 and 2.

2.3. Part 3: performance of the final questionnaire

2.3.1. Data analysis

Acceptability was assessed by considering the proportion of respondents completing the lengthy draft questionnaire. Construct validity was assessed by considering the fit between the results of the factor analysis and the results of the initial qualitative work, and by considering the potential overlap between questionnaire items and those depressive symptoms captured by the BDI-II. We conducted a sensitivity analysis of the results of the factor analysis of Sections 1and 2. The 20 items from Sections 1 and 2, and all 21 items comprising the BDI-II, were entered into a principal components factor analysis, to determine whether the factor analysis output was similar to the original without the BDI-II items. If this was the case, the original solution was robust, and it would support the hypothesis that the questionnaire and the BDI were measuring different phenomena. Internal consistency reliability was assessed for the total score, and for each domain and sub-total, using Cronbach's reliability coefficient alpha. We also calculated Cronbach's alpha if each item was deleted, to check that this did not lead to an increase in any instance. By convention, alpha should be at least 0.70 in an 'adequate' scale, and more than 0.80 is desirable. Split-half reliability was determined for each dimension, subtotal and total, by calculating Guttman's split half coefficient. Test–retest reliability was determined for each dimension, subtotal and total, by calculating intraclass correlation coefficients. Finally, sensitivity to change was assessed.

3. Results

3.1. Part 1: creation of a draft questionnaire

After initial piloting of a draft questionnaire, the questionnaire was split into three different sections, each of which contained different types of item.

- Section 1 asks participants to rate the extent of their agreement with statements describing specific aspects of their emotional experience during the past week. It includes statements such as 'I don't get angry, irritated or aggressive', 'sometimes my emotions are more like thoughts than feelings' and 'I don't care much about other people's opinions of me'. It also includes statements which necessarily require participants to make subjective judgements about the 'normality' of their experiences, such as 'I don't care about my day to day responsibilities as much as I should', 'sometimes I feel that I should cry, but I don't', and 'I don't fully enjoy things that should give me pleasure, such as beautiful places or things or music'. These statements reflect the way in which participants described their emotional side-effects during qualitative interviews.
- Section 2 asks participants to rate the extent of their agreement with statements *comparing* their emotional experiences *during the past week* with those *before they developed their illness/problem*, such as 'Day to day life just doesn't have the same emotional impact on me that it did before my illness/problem'. This reflects the way in which many participants in the preparatory qualitative study (Price et al., 2009) described their altered emotional experiences, by contrasting them with a previous time.
- Section 3 first asks whether the participant is currently prescribed antidepressants for their illness/problem, and, if they are not, asks them not to answer any more questions. The items address the extent to which participants attribute their emotional difficulties to their antidepressant, and the extent to which they would therefore be considered by participants to be 'emotional side-effects'. The last two items address poor antidepressant compliance due to 'emotional side-effects'.

The draft questionnaire comprised 78 items, of which 50 were in Section 1, 15 in Section 2, and 13 in Section 3. A copy is available from the corresponding author.

3.2. Part 2: refinement of the draft questionnaire

3.2.1. Nature of the sample

207 participants completed a questionnaire on at least one occasion. Table 1 outlines the demographic characteristics of these participants, and their BDI-II scores at week 0. Table 2 outlines the antidepressant classes taken by the participants at week 0, and the duration of their antidepressant use. Reported antidepressant adherence was high, with 179 (87%) reporting that they took their antidepressant every day, and 23 (11%) on most days. No participants reported taking St John's Wort, but 16 (8%) were taking a mood stabiliser and 41 (20%) another psychotropic medication.

Table 1
Characteristics of participants.

Gender — n (%)	Male	47 (23%)
	Female	160 (77%)
Age — years	Minimum	20
	25% Quartile	27
	Median	38
	75% Quartile	52
	Maximum	87
	Mean	41.3
	SD	16.1
Residence — n (%)	In Oxfordshire	127 (61%)
	Outside Oxfordshire	80 (39%)
BDI-II scores	Minimal depression (0–13)	75 (36%)
	Mild depression (14–19)	44 (21%)
	Moderate depression (20–28)	37 (18%)
	Severe depression (29–63)	51 (25%)
	Mean	19.3
	SD	12.8

Table 2
Antidepressant use at week 0.

		n (%)
Nature	SSRI	137 (66%)
	SNRI	33 (16%)
	TCA/TCA-related	19 (9%)
	Combination	13 (6%)
	Others	5 (2%)
	MAOI	0 (0%)
Duration	<1 week	2 (1%)
	1–4 weeks	9 (4%)
	4 weeks–3 months	21 (10%)
	3 months–6 months	23 (11%)
	6 months–12 months	37 (18%)
	>12 months	115 (56%)

3.2.2. Gold standard question

Fifty three participants (26%) reported that they experienced no emotional side-effects during the previous week, and 32 (16%) reported insignificant, 62 (30%) mild, 47 (23%) moderate and 13 (6%) severe emotional side-effects. Table 3 compares the characteristics of participants with and without emotional side-effects (mild/moderate/severe vs nil/insignificant on the gold standard question). Participants with emotional side-effects were younger, had higher BDI-II scores, had shorter treatment duration, and were less likely to live outside Oxfordshire, but were of similar gender.

3.2.3. Sections 1 and 2: exclusion of items prior to factor analysis

We excluded from the initial factor analysis 15 of 50 items in Sections 1 and 2 of 15 items in Section 2 of the draft questionnaire, on the basis of key performance statistics (ceiling or floor effect; kappa and Kendall's tau-b from cross-tabulation with gold standard question; corrected item–total correlation).

3.2.4. Sections 1 and 2: factor analysis

Iterative factor analysis leads to the factor solution detailed in Table 4, in which 20 questionnaire items are grouped into four dimensions to generate Sections 1 and 2 of the final questionnaire. The varimax rotation converged in seven iterations. After rotation, factor 1 ('not caring') explains 17.8% of the variance, factor 2 ('general reduction') 17.4% of the variance, factor 3 ('emotional detachment') 16.6% of the variance, and factor 4 ('positive reduction') 15.9% of the variance. These four factors therefore explain 67.6% of the variance. Other factors were excluded from the solution as they had eigenvalues of <1.00.

3.2.5. Section 3: factor analysis

We excluded from the initial factor analysis 3 of 13 items in Section 3 of the draft questionnaire, on the basis of key performance statistics. These items were a) the only reverse polarity item (ceiling effect, low item–total correlation), b) the item relating to reduction in negative emotions (and therefore akin to the results of the analysis of Sections 1 and 2 items) (low item–total correlation), and c) the item relating to stopping the antidepressant (floor effect, low item–total correlation).

Table 5 details the results of the initial factor analysis for Section 3 items. Seven of the ten items loaded to a dimension which we call 'my antidepressant causes emotional side-effects' (AC). Of these seven items, four (3:05, 3:06, 3:08, and 3:10) represented the four dimensions resulting from the factor analysis of Sections 1 and 2. One (3:04) was akin to emotional detachment from others, but was more specific than item 3:06, and so was excluded in favour of 3:06. Items 3:07 and 3:03 had lower loadings than the other five items, and so were excluded in favour of a five item solution. The remaining three items loaded to a dimension which we call 'the problem is my antidepressant not my illness' (PA). Two items (3:02 and 3:11) appeared to overlap in meaning, and item 3:11 was excluded in favour of 3:02 as it had a lower loading.

Table 3
Comparison of participants with and without self-reported emotional side-effects (gold standard question).

	With emotional side-effects (Mild/moderate/severe)	Without emotional side-effects (Nil/insignificant)	Comparison	*p*
Age, years — median (IQR)	35 (27–49)	44 (29–60)	Mann Whitney U 4155.0, Z = −2.430, 2 tailed	0.015
BDI-II score — median (IQR)	23 (15–35)	9 (4–17)	Mann Whitney U 1997.0, Z = −7.523, 2 tailed	0.001
Antidepressant treatment duration <6 months — %	33	18	Chi-square 5.89, df = 1, 2 tailed	0.015
Live in Oxfordshire — %	52	75	Chi-square 11.82, df = 1, 2 tailed	0.001
Male gender — %	28	22	Chi-square 0.10, df = 1, 2 tailed	0.920

Table 4
Results of final factor analysis: item loadings and components.

Questionnaire item		Component				Qualitative theme	Final dimension
		1	2	3	4		
1: 43	Because I don't care so much about things, I'm having problems at work or college	0.799				Not caring	Not caring (NC)
2: 08	I don't care as much about my day to day responsibilities as I did before I developed my illness/problem	0.790				Not caring	
2: 10	I just don't care about things as much as I did before my illness/problem	0.702				Not caring	
1: 48	I feel spaced out and distant from the world around me	0.655				Detachment	
1: 26	Because I don't care so much about things, I'm having problems at home	0.654				Not caring	
2: 03	My emotions are numbed/dulled/flattened compared to before I developed my illness/problem		0.812			General reduction	General reduction in emotions (GR)
2: 02	Day to day life just doesn't have the same emotional impact on me that it did before my illness/problem		0.743			General reduction	
1: 16	Unpleasant emotions, such as sadness, disappointment, and upset, feel toned down or different in some way		0.733			Negative reduction	
1: 01	All my emotions, both 'pleasant' and 'unpleasant', are 'toned down'		0.708			General reduction	
1: 22	My emotions lack intensity		0.708			General reduction	
1: 13	I don't have much sympathy for people			0.812		Detachment	Emotional detachment from others (ED)
1: 10	I care less about other people's feelings than I think I should			0.779		Detachment	
1: 23	Other people being upset doesn't affect me			0.778		Detachment	
2: 15	I don't have as much sympathy for other people as I did before my illness/problem			0.736		Detachment	
2: 14	I don't react to other people's emotions (such as their sadness, anger or upset) as much as I did before my illness/problem			0.663		Detachment	
1: 03	I don't fully enjoy things that should give me pleasure, such as beautiful places or things or music				0.777	Positive reduction	Reduction in positive emotions (PR)
1: 19	I don't look forward to things with eager anticipation				0.701	Positive reduction	
2: 09	I don't get as much of a 'high' from good things in my life as I did before my illness/problem				0.696	Positive reduction	
1: 11	I don't have the passion and enthusiasm for life that I should				0.675	Positive reduction	
2: 05	I don't experience pleasant emotions as much as I did before I developed my illness/problem				0.581	Positive reduction	

3.2.6. The final questionnaire

The final Oxford Questionnaire on the Emotional Side-effects of Antidepressants (OQuESA) is attached as an Appendix. It comprises three sections. Section 1 comprises 12 items, three from each of the four dimensions derived from qualitative research: 'not caring (NC)', 'emotional detachment (ED)', 'positive reduction (PR)', and 'general reduction (GR)'. Section 2 comprises 8 items, two from each of the four dimensions. Section 3 is for completion only by those respondents currently prescribed antidepressants for their illness/problem, and respondents who do not fulfil this criterion are eliminated at this point by a screening question. Section 3 comprises 6 items which ask the respondent about their beliefs about their emotional side-effects and their antidepressant. Four items relate to the dimension 'my antidepressant causes emotional side-effects', and each item

Table 5
Results of initial factor analysis of Section 3.

Questionnaire item		Component		Comments
		1	2	
3: 08	AD is preventing me from feeling pleasant emotions	0.794		= Positive reduction
3: 05	AD seems to make me just not care about things that should matter	0.792		= Not caring
3: 04	AD makes me less able to feel affection/love for those close to me	0.786		= Emotional detachment, but specific rather than general item
3: 06	AD seems to make me feel disconnected from people and things around me	0.744		= Emotional detachment, but general rather than specific item
3: 10	AD is preventing me from feeling my emotions in some way	0.714		= General reduction
3: 07	AD has helped my illness, but left me feeling a different person	0.698		Excluded; lower loading
3: 03	AD prevents me from feeling emotions in the way that it should	0.695		Excluded; lower loading
3: 12	Have considered stopping AD due to ESEs		0.826	Stopping antidepressant
3: 02	AD changes my emotions in an unhelpful way just now		0.778	Antidepressant is unhelpful
3: 11	Problems with my emotions seem to be due to my AD rather than the illness		0.737	Antidepressant is unhelpful, but lower loading; exclude

Extraction method: Principal Component Analysis. Rotation method: Varimax with Kaiser Normalization. Rotation converged in 3 iterations.

relates to one of the four dimensions. Two items relate to the dimension 'my problem is my antidepressant not my illness', such as 'the antidepressant changes the way that I experience my emotions in a way that is unhelpful (not helpful) to me at the moment'. Information on how to score the OQuESA is available from the corresponding author.

3.3. Part 3: performance of the final questionnaire

3.3.1. Acceptability

Completion of the draft questionnaire was high, with 207 available at week 0, 205 at week 1, and 199 at week 4. Online completion was our preferred mode of administration, and 170 participants (82%) used this method at week 0, with 37 participants preferring paper. At week 0, 206 out of 207 participants completed all 78 questions of the draft questionnaire, and the other participant completed all questions apart from those in Section 2. Anecdotally, there were few difficulties with online completion, and the ease of use and reliability of the online data entry form appeared to be very high. The median time period between completion of the week 0 and week 1 questionnaires was 7 days (IQR 7–8), and between the week 1 and week 4 questionnaires was 21 days (IQR 21–24).

3.3.2. Construct validity

Table 4 lists, for each questionnaire item, the qualitative theme from which it was derived (Price et al. 2009), and the final dimension to which it contributes. Generally, there was strong correspondence between the themes, derived qualitatively, and the final dimensions of the questionnaire, derived quantitatively.

The dimensions ED and GR were weakly positively correlated with BDI-II scores, with Kendall's tau-b correlations each of 0.22, whereas the dimensions PR and NC were moderately positively correlated, with correlations each of 0.54. The relationship between depressive symptoms and OQuESA items was further explored in a sensitivity-type analysis by conducting a principal components factor analysis in which both the 20 items within Sections 1 and 2 of the final OQuESA

Table 6
Results of factor analysis entering a) final questionnaire items and b) all BDI-II items, listing only loadings >0.500.

Questionnaire item			Component						
			1	2	3	4	5	6	7
BDI: 03c		Past failure	.745						
BDI: 14c		Worthlessness	.744						
BDI: 02c		Pessimism	.716						
BDI: 07c		Self-dislike	.715						
BDI: 08c		Self-criticalness	.667						
BDI: 06c		Punishment feelings	.644						
BDI: 05c		Guilty feelings	.615						
1:11	PR	I don't have the passion and enthusiasm for life that I should	.526						
BDI: 13		Indecisiveness	.526						
BDI: 01		Sadness	.500						
1:03	PR	I don't fully enjoy things that should give pleasure, such as …							
BDI: 10		Crying							
1:01	GR	All my emotions, both 'pleasant' and 'unpleasant', are toned down		.792					
1:22	GR	My emotions lack intensity		.783					
1:16	GR	Unpleasant emotions, such as …, feel toned down or different in some way		.755					
2:03	GR	My emotions are numbed/dulled/flattened compared to before …		.734					
2:02	GR	Day to day life just doesn't have the same emotional impact as it did …		.586				.519	
2:09	PR	I don't get as much of a 'high' from good things in my life as I did before …		.533					
2:05	PR	I don't experience pleasant emotions as much as I did before …		.527					
1:19	PR	I don't look forward to things with eager anticipation							
BDI: 11		Agitation			.733				
BDI: 18		Changes in appetite			.648				
BDI: 17		Irritability			.643				
BDI: 19		Concentration difficulty							
BDI: 09c									
1:13	ED	I don't have much sympathy for other people				.810			
1:23	ED	Other people being upset doesn't affect me				.788			
1:10	ED	I care less about other people's feelings than I think I should				.784			
2:15	ED	I don't have as much sympathy for other people as I did before …				.737			
2:14	ED	I don't react to other people's emotions (such as …) as much as I did before …				.669			
BDI: 15		Loss of energy					.793		
BDI: 20		Tiredness or fatigue					.719		
BDI: 12		Loss of interest					.501		
BDI: 04		Loss of pleasure							
BDI: 16		Changes in sleeping pattern							
2:08	NC	I don't care as much about my day to day responsibilities as I did before …						.683	
2:10	NC	I just don't care about things as much as I did before my illness/problem						.624	
1:43	NC	Because I don't care so much about things, I'm having problems at work or college						.515	
1:48	NC	I feel spaced out and distant from the world around me							
BDI: 21		Loss of interest in sex							
1:26	NC	Because I don't care so much about things, I'm having problems at home							

Extraction method: Principal Component Analysis. Rotation method: Varimax with Kaiser Normalization. Rotation converged in 9 iterations.

and all 21 BDI-II items were entered. The loadings of each item are reported in Table 6, when absolute loading values were above 0.5. The dimensions ED and GR are *unaffected* by the introduction of the 21 depression items, in that a) the included five items remain together in the same dimension, and b) no depression items load to the dimensions with an absolute value of >0.5. The dimensions NC and, particularly, PR, are, however, *affected* by the introduction of the depression items. The five NC items have lower loadings than the ED and GR items, and much lower than in the final factor analyses without depression items. The five PR items have lower loadings than items from other dimensions, which are also much lower than in the final factorial analysis without depression items. In addition, they appear to contribute to a dimension dominated by BDI-II items, of which 'past failure', 'worthlessness', 'pessimism' and 'self-dislike', and other so-called 'cognitive items' of the BDI, are prominent.

3.3.3. Internal consistency reliability

The Cronbach's alpha statistic was 0.87 for the ED dimension, 0.88 for GR, 0.86 for PR, and 0.87 for NC; 0.89 for the subtotal ED-GR, and 0.90 for PR-NC; and 0.93 for the total score. In each of the dimensions, subtotals, and the total score, Cronbach's alpha is above 0.80, and therefore, by convention, internal consistency reliability would be seen as 'good'. The Cronbach's alphas for the dimensions if each item was separately deleted were also calculated. No item, if deleted, would lead to an increase in the Cronbach's alpha for its particular dimension.

3.3.4. Split-half reliability

Guttman's split half coefficient was 0.81 for the ED dimension, 0.78 for GR, 0.80 for PR, and 0.82 for NC; 0.69 for the subtotal ED-GR, and 0.79 for PR-NC; and 0.88 for the total score. It would therefore be considered adequate or good for each dimension, subtotal and total.

3.3.5. Test–retest reliability

Intra-class correlation between scores at week 0 and week 1 was 0.85 for the ED dimension, 0.80 for GR, 0.86 for PR, and 0.84 for NC; 0.88 for the subtotal ED-GR, and 0.89 for PR-NC; and 0.90 for the total score. These correlations are above 0.8, and would therefore be considered good.

3.3.6. Sensitivity to change

For the 62 participants whose gold standard response *decreased* by one or more points between weeks 0 and 4, the mean reduction in OQuESA total score was 4.61, and a paired *t* test indicated that this was a statistically significant change (mean reduction 4.61, 95% CIs 1.77–7.46, $t=3.24$, $df=61$, $p=0.002$ (2 tailed)). For the 38 participants whose gold standard response *increased* by one or more, the mean increase in OQuESA total score was 2.81, but this did not reach statistical significance (mean increase 2.81, 95% CIs 5.72 to −0.99, $t=1.96$, $df=36$, $p=0.058$ (2 tailed)). For the 99 participants whose gold standard response *did not change*, the total score increased by 0.980, which was not statistically significant (mean increase 0.980, 95% CIs −1.06 to 3.01, $t=0.956$, $df=98$, $p=0.342$).

4. Discussion

4.1. Main findings

We have developed a patient-centred, self-report measure of emotional symptoms present in patients treated with antidepressants (The Oxford Questionnaire on the Emotional Side-effects of Antidepressants, OQuESA): it can be completed either on paper or online. The OQuESA appears to be a highly acceptable, valid and reliable measure, with sensitivity to change. Our results suggest that the OQuESA measures one or more aspects of depression, rather than necessarily measuring only emotional effects mediated by antidepressants. Thus, scores are highest in patients who are depressed. Patients also endorse items on the questionnaire when apparently in remission, which has two possible interpretations. Either, in remission, such symptoms are present because they are untreated or they are present because they are produced by antidepressants. We must leave open the question of which interpretation is correct until appropriate double blind studies are completed; such studies, using the OQuESA, are currently under way.

The OQuESA has high acceptability: despite the draft OQuESA comprising 78 items, attrition was low, with 95% of participants completing it at each of three time-points. Most questionnaires were completed online, and therefore this mode of administration appears to be acceptable.

The OQuESA has high construct validity — four of the seven themes identified in the qualitative study (Price et al., 2009) are represented in the OQuESA as dimensions (PR — reduction in positive emotions, GR — general reduction in emotions, NC — not caring, and ED — emotional detachment). In addition, OQuESA items are closely related to the contents of the Laukes Emotional Intensity Scale (LEIS) — care about others' feelings, for example, is identical to item 1:3 ('I care less about other people's feelings than I think I should'), and sadness is a component of item 1:5 ('Unpleasant emotions, such as sadness, disappointment, and upset, feel toned down or different in some way'). Finally, the five items comprising the other existing measure, the Bell–Shipman Apathy Questionnaire, fits well within the thematic framework derived from our qualitative study, and also fits well with the OQuESA items. For example, BSAQ item 5 ('Lately, I notice that things that I used to be enthusiastic about – things that used to get me excited or stimulated – no longer cause me to feel enthusiastic, excited or stimulated') is closely akin to the dimension PR, and therefore to items 1:2, 1:6, 1:10, 2:2 and 2:6.

In the qualitative study, considerable effort was expended in attempting to 'unpick' the distinction between the 'emotional blunting' which arises in the context of depressive illness (e.g. reduced pleasurable emotions, reductions in caring) and the 'emotional blunting' which may be a side-effect of antidepressant medication. That this was challenging is supported by the significant correlation between level of depressive symptoms and OQuESA total score, each of the dimensions of the OQuESA, and, in particular, the dimensions PR and NC. This makes intuitive sense — PR and NC are experiences that are more closely allied with the symptoms of depression than GR and ED, and aspects of the OQuESA may therefore be measuring an aspect of depression, rather

than an adverse effect of a treatment of depression. The sensitivity analysis, conducted by repeating the factor analysis with depression items included, supports this conclusion: the dimensions ED and GR appear to be distinct from BDI-II-defined depression, being unaffected by the introduction of those depression items. By comparison, the dimensions NC and PR are affected and, indeed, the dimension PR appears closely related to the cognitive conceptualisation of depression embodied in the 'cognitive' items of the BDI-II. This has lead to our recommendation that, when dimension scores are combined, they lead not only to a final summed score but also to two sub-totals (ED-GR and NC-PR).

The OQuESA has high reliability. The OQuESA's internal consistency reliability was high, i.e. items within each construct were highly (but not too highly) correlated, each item contributed similarly to each dimension, and all items were coded in the correct direction. Splitting the OQuESA randomly into two did not unduly affect its functioning (split-half reliability). Finally, OQuESA scores were similar when administered a week apart (test–retest reliability).

The OQuESA appears sensitive to change, but this needs further confirmation from naturalistic and randomised studies.

4.2. Strengths and limitations of the study

The study has three key strengths. First, all the items comprising the draft questionnaire and, therefore, all the items comprising the final OQuESA, were derived directly from patients. Second, the statistical procedures used to refine the draft OQuESA and evaluate the final OQuESA were comprehensive and of high quality. Finally, the sample was large and disparate, comprising participants on a wide variety of antidepressants, with wide variation in self-reported emotional side-effects of antidepressants, and wide variation in self-reported depressive symptoms.

The main limitation relates to the absence of a gold standard measure of emotional blunting, and, therefore, the difficulty in evaluating its 'accuracy'. Related to this, the success of the 'gold standard question' relies, in each participant, on their successful interpretation and application of our words to their own emotional experiences. While we have good evidence from the qualitative study (Price et al., 2009) that this is possible, it is likely that some participants will have found this process difficult. Furthermore, this study's participants were defined by their use of antidepressants, rather than by a mood disorder diagnosis, and did not receive a formal diagnostic interview. We therefore do not know what proportion had current or lifetime mood disorder.

In healthy volunteers taking antidepressants, emotional blunting has not been reported. The necessary experiment has probably not been conducted over sufficient time. Healthy volunteers given paroxetine 20 mg over 8 weeks clearly experience marked sexual dysfunction (Montejo et al., 2010) but the maximal effect was not seen before 4 weeks. We await a definitive study of the effects of a SSRI on emotional experience per se. Meanwhile, any interpretation must allow that emotional blunting is currently only associated with being depressed, and given the overlap with depressive symptoms, depression may be a necessary pre-condition to see the phenomenon even if it is precipitated by drug treatment.

4.3. Implications

The OQuESA represents a significant advance over the two existing instruments – the LEIS (described in Opbroek et al., 2002) and the BSAQ (Bell et al., 2006) – which claim to measure emotional blunting in the context of antidepressant use. The OQuESA comprises items derived from an in-depth qualitative study of patient experience of emotional blunting; is comprehensive, with 26 items across three complementary sections; and has been validated in a diverse group of over 200 antidepressant users.

The OQuESA may help clinicians to assess patients with depression who present with troubling residual symptoms, and to track their progress in response to clinical interventions such as psychological therapy or change of pharmacotherapy.

Further research on the OQuESA should be focused in three areas:

a. Determination of the frequency and severity of emotional blunting in a variety of patient populations, sampled in a variety of ways. The OQuESA should allow, for example, comparison of emotional blunting with specific antidepressants, and comparison across antidepressant classes. This will extend to the assessment of new antidepressants within randomised controlled trials, and potential new antidepressants in earlier, more exploratory, research.
b. Determination of the frequency and severity of emotional blunting in healthy volunteers treated with antidepressants, to help understand whether emotional blunting is related to residual depression or to antidepressant side-effects.
c. Translation of the OQuESA into other languages, and the establishment of the reliability and validity of these versions.

5. Conclusion

The OQuESA offers promise as an effective self-report measure of the symptoms of emotional blunting in patients with depression. Our hypothesis is that it captures novel aspects of depressive mood — either residual symptoms that remain after 'successful' treatment with antidepressants, or emotional side-effects of antidepressant treatment. The OQuESA can be used as a clinical tool, to facilitate the identification of patients with the syndrome of emotional blunting. It should also be used in research studies, to advance our understanding of the nature, causes and treatment of this phenomenon.

Role of funding source

Servier, the funder, have a research programme for the development of psychotropic compounds, including antidepressants. Servier were able to comment on initial study design, but had no role in the collection, analysis and interpretation of data, and no role in the writing of the manuscript, although they were able to comment on the final manuscript. They had no influence on the decision to submit the paper for publication. The researchers were, therefore, independent of the funders.

Conflict of interest

J.P. has received grants and honoraria from Servier. G.G. has received grants from Sanofi-Aventis and Servier in the past and recent honoraria from AstraZeneca, BMS, Eisai, Lundbeck MSD and Servier. He has advised AstraZeneca, BMS, Lilly, Lundbeck, P1Vital and Sanofi-Aventis, Servier and Wyeth. H.D. has no conflicts of interest. V.C. has no conflicts of interest.

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