

# Negative bias in interpretation and facial expression recognition in late life depression: a case control study

## Running title

Negative bias in in late life depression

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## Data availability

Consent to upload data onto open platforms was not obtained for this study. Anonymous data can be shared with other research groups who have ethical approval in place on a by-project basis. Requests for data access should be made to the corresponding author.

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## Conflict of interest disclosure

PW is a member of the UK National Institute for Health and Care Excellence (NICE) Depression in Adults (update) Guideline Development Committee. SEM has received consultancy fees from P1Vital Ltd, Janssen Pharmaceuticals, Zogenix and Sumitomo and holds grant income from UCB Pharma, Janssen Pharmaceuticals and Zogenix. MB has received travel expenses from Lundbeck for attending conferences and has acted as a consultant for Jansen Research and CHDR. NB, SB and TB have no interests to declare.

## Ethics approval

The study was approved by the UK Health Research Authority and the London City and East Research Ethics Committee (reference 16/LO/1184). The study was conducted in accordance with the principles of the Declaration of Helsinki and in full conformity with the ICH Guidelines for Good Clinical Practice (CPMP/ICH/135/95) July 1996

## Patient consent

Written informed consent was obtained from all participants before participation in the study

## **Abstract**

**Objectives:** While cognitive bias in younger adults with depression has been extensively researched, there have been relatively few investigations of the presence of cognitive bias in late life depression (LLD). This exploratory study aimed to ascertain whether negative cognitive bias exists across a range of cognitive domains in participants with LLD.

**Methods/Design:** Participants were 19 patients with LLD and 19 matched non-depressed older adults. Participants completed standardised tests to assess bias in facial expression recognition, attention, recall of adjectives and interpretation.

**Results:** LLD participants were slower to identify surprised faces, and more likely to create negative statements in the interpretation task. There was no evidence of negative bias in memory or attention, but participants with LLD performed more poorly on the recall task.

**Conclusions:** This study provides new evidence of negative bias in interpretation in LLD, but the findings are not consistent with a global cognitive bias. Further work is needed to investigate cognitive bias in LLD. It may be that interventions which target negative interpretation biases, such as cognitive bias modification, could be helpful in treating LLD.

## **Key words**

Late life depression, negative cognitive bias, facial expression recognition, interpretation

## **Key points**

1. Participants with LLD showed negative cognitive bias in interpretation
2. Participants with LLD showed a poorer performance in recall of adjectives and identification of surprised expression but there was no evidence of bias.
3. There was no evidence of cognitive bias in attention in LLD.
4. Negative bias in interpretation is associated with LLD. Further work to establish the effectiveness of cognitive bias modification in this group would be useful.

## Introduction

Depression is common in older adults<sup>1</sup>, but our understanding of its aetiology is limited<sup>2,3,4</sup>, which hampers treatment development<sup>5,6,7</sup>. “Negative cognitive bias” describes the tendency of certain individuals to preferentially process negative at the expense of positive information. Negative biases play a pivotal role in cognitive models of depression, where they are argued to be causal factors in the onset and maintenance of symptoms of the illness<sup>8</sup>. Consistent with these models, there is evidence to suggest that depressed younger adults selectively attend to negative stimuli<sup>9,10</sup>, have a better memory for negative material than for positive or neutral material<sup>8,11</sup>, and interpret ambiguous stimuli negatively<sup>12,13</sup>. While cognitive bias in younger adults with depression has been extensively researched, there have been relatively few investigations in this area in late life depression (LLD) and existing evidence is mixed.

A negative attentional bias has been demonstrated in some studies of LLD and remitted patients using both the emotional Stroop and dot-probe tasks,<sup>6,7,14</sup> although this was not demonstrated by Mah and Pollock (2009)<sup>3</sup>.

There is mixed evidence for negative bias in memory in LLD with both positive<sup>4,5</sup> and negative<sup>5,15</sup> findings reported.

Other studies have investigated identification of facial expressions in LLD and after remission of depression<sup>16-18</sup>. People with LLD have been found to be both less accurate at identifying positive expressions and more accurate at identifying negative expressions<sup>16,17,18</sup> and more likely to interpret ambiguous expressions as being negative<sup>19</sup>. In one study of patients with LLD, identification accuracy for positive expressions improved with antidepressant treatment which also predicted a better response to antidepressants<sup>17</sup>. However, other studies have shown either no bias<sup>20</sup> or reduced accuracy for negative faces<sup>21</sup>. Interpretation bias in non-face stimuli has not, to our knowledge, been previously investigated in LLD.

In summary, a number of studies have reported negative cognitive bias in LLD<sup>4-7,14-19</sup> but these findings are not consistently replicated<sup>3,15,20,21</sup>. To date, studies have tended to use measures of bias limited to a single cognitive domain, such as memory, attention or interpretation, sometimes in non-clinical groups. The current exploratory study aimed to measure bias across a range of cognitive domains using a standardised battery of cognitive tests, in a clinical sample of participants with a

confirmed diagnosis of LLD. It was hypothesised that participants with LLD would show negative cognitive biases in measures of facial expression recognition, attention, interpretation and memory, when compared with non-depressed controls (task specific definitions of negative bias are provided in the appendices).

## Methods and Materials

A case control design was used. Following a brief telephone screening call, participants were invited to attend a single study visit during which a clinical interview, standard questionnaires and computerised tasks measuring cognitive bias were completed. All participants were reimbursed for expenses and participants in the control group also received monetary compensation for their time. Written informed consent was obtained before participation. The study was approved by the UK Health Research Authority and the London City and East Research Ethics Committee (reference 16/LO/1184). 19 participants with a diagnosis of LLD and 19 matched non-depressed controls were recruited in Oxfordshire and Buckinghamshire over a two-year period (see figure 1). Participants with a clinical diagnosis of LLD (made by their psychiatrist or GP based on ICD 10 criteria) were recruited from primary and secondary care including community and inpatient psychiatric teams. Non-clinical control participants were recruited from the local community through advertising, or they were contacted directly using the Oxford Cognitive Health in Ageing healthy volunteers register (OxDARE). This is a database of volunteers who are willing to be contacted about research. Inclusion criteria were: current episode of major depression (LLD group) and no current or previous axis 1 or substance misuse disorder (LLD and control groups) using the Mini-International Neuropsychiatric Interview<sup>22</sup> (MINI); aged 60 years or over; sufficiently fluent in English to understand the task and instructions; and able to use simple computer keyboard functions. Exclusion Criteria were: ICD10 diagnosis of dementia made by the patient's own clinician; diagnosis of bipolar disorder using the MINI; familiarity with tasks used in the study; a current severe medical condition; significant doses of sedative medication, such as benzodiazepines, which in the researcher's opinion would impair a participant's ability to complete the study tasks.

One control per case was recruited. Controls were selected to be as closely matched to depressed participants as possible on age, sex, level of education and cognitive function. Attempts were made to match cognitive function between groups through matching age and level of education, but it was not possible to exactly predict MOCA scores in control participants in advance. Participants also completed the Hamilton Depression Rating Scale (HDRS)<sup>23</sup> and the State-Trait Anxiety Inventory (STAI)

at baseline<sup>24</sup>. Cognitive function was assessed using the Montreal Cognitive Assessment (MOCA)<sup>25</sup> and educational level using the National Adult Reading Test (NART)<sup>26</sup>.

Participants were then asked to complete cognitive tests to assess cognitive bias across different cognitive domains. Facial expression recognition, attention and recall of adjectives were assessed using the P1vital Emotional Test Battery (ETB) set of tasks<sup>27</sup> and interpretation was assessed using the scrambled sentences task<sup>28</sup>. The ETB<sup>27</sup> is designed to assess the processing of a variety of affectively valenced stimuli and comprises four validated, computerised cognitive tasks: Facial Expression Recognition Task (FERT), Emotional Categorisation Task (ECAT), Facial Dot-Probe Task (FDOT) and Emotional Recall Task (EREC). The ETB is well used in studies of negative cognitive bias in depression and is sensitive to cognitive bias in depression and to the effects of treatments for depression<sup>29-32</sup>, and has shown test-retest reliability<sup>27</sup>. Questionnaires and cognitive tasks were all administered by members of the research team who were not blinded to participant group.

The FERT comprises a series of facial expressions associated with six basic emotions: anger, disgust, fear, happy, sad and surprise in a range of different intensity levels. Participants were required to identify the emotion of the face. Outcome measures were accuracy, percentage of misclassifications and mean reaction time for correct responses for each emotion. The ECAT comprises a series of positively and negatively valenced self-referent words, and participants were required to indicate whether they would like or dislike to be referred to as each word. Outcome measures were again accuracy and mean reaction times.

In the FDOT, participants reported the orientation of two dots - whether the two dots were aligned horizontally (..) or vertically (:). The dots appeared in a random position on the screen and were preceded by an emotional face (fearful or happy) or a neutral face. Reaction times were recorded. A measure of attentional bias, the vigilance score, was the outcome measure. This is calculated by comparing the reaction times from congruent trials (trials where the probe appears in the same location as the stimulus) from incongruent trials (trials where the probe appears in a different location from the stimulus). The EREC is a surprise recall task during which participants were required to remember as many of the positively and negatively valenced self-referent words from the ECAT as they could in four minutes. Outcome measures were the number of words correctly recalled and the number of words falsely recalled (false alarms). In the scrambled sentences task<sup>28</sup>, participants were presented with 20 strings of six words and asked to rearrange them to make a five word sentence, within a four minute time limit. Positive or negative sentences could be created. The number of

negative sentences created was divided by the total number of correct sentences to get a measure of negative bias in interpretation, the negativity score. (Please see Appendices for further details of all tests used).

## **Analysis**

Statistical analyses were performed using SPSS v. 27. Baseline differences between the study groups were tested using t-tests and chi-squared tests as appropriate. Differences between the study groups on the FERT, ECAT, EREC and FDOT tasks were examined using repeated measures ANOVAs. Group was a between-subject factor, task conditions were within-subject factors and group matching measures (age, MOCA, gender and years of education) were included as control variables. As a number of tasks showed a difference between groups we performed post-hoc correlations of the scores on these tasks specifically within the LLD group. The rationale for these analyses were to assess for evidence that the various tasks were measuring the same underlying bias vs. distinct, modality specific biases. Where assumptions of sphericity were not met, the Greenhouse-Geisser correction was used.

Within-subject factors were as follows: on the FERT: emotional valence (happy, sad, fear, surprise, disgust, anger); on the FDOT: masking (masked, unmasked), valence (positive, negative), and congruency (congruent [dot probe replaces emotional face] and incongruent [dot probe replaces neutral face]); and on the ECAT and EREC: valence (positive, negative). For the scrambled sentences task negativity scores were compared using a univariate ANOVA with group as a between-subject factor and covariates included as above. Dependent variables on the tasks were as follows: FERT: accuracy, misclassifications, reaction times; FDOT: reaction times; EREC: number of adjectives correctly recalled, number of false alarms; ECAT: accuracy and reaction times; scrambled sentences: negativity score. Participants were excluded for the following reasons: on the FERT one LLD participant did not meet the minimum number of correct responses (the a priori cut-off for the minimum number of correct responses on this task is 50), on the FDOT the computer crashed during the task for one LLD participant, and on the scrambled sentences task one LLD participant was unable to complete due to tremor and one control declined to do the task because they were too tired.

A level of significance of  $p < 0.05$  was adopted. No correction for the number of tasks analysed was made. The study aimed to provide a broad and initial description of different cognitive biases across

different cognitive domains, and avoiding type two errors was therefore prioritised in this exploratory study.

Seven participants with LLD were taking potentially sedative medications which may have generally impaired task performance. In order to test whether identified group differences could be accounted for by the effect of these medications, sensitivity analyses were performed in which these participants were excluded. Group matching measures were included as covariates of no interest in all analyses to control the effects of these variables on differences between groups in performance. We report significant effects of control variables in the appendix.

## Results

90 potential participants were screened, 33 were excluded and 19 declined to participate. Of the potential LLD participants who were excluded (n=21) 1 was too depressed to consent, while 20 did not meet criteria for major depression (see Figure 1). The depressed participants were recruited from primary (n=4) and secondary care (n=15). Of the patients receiving input from secondary care 6 were inpatients and 9 were under community mental health teams Demographic characteristics of the study sample (n=38) are presented in table 1 and clinical details of the depressed group (n=19) in table 2.

(Table 1)

There were no significant differences in age ( $t=-0.302$ ,  $df=36$ ,  $p=0.7$ ), gender (chi square=0,  $df=1$ ,  $p=1$ , years of education or NART ( $t=-1.111$ ,  $df=36$ ,  $p=0.274$ ) between the groups. MOCA scores in depressed participants were significantly lower than those in controls ( $t=-2.137$ ,  $df=36$ ,  $p=0.039$ ). Measures of depression and anxiety differed significantly in the expected direction between depressed participants and controls ((HDRS  $t=19.2$ ,  $df=35$ ,  $p<0.001$ ; one missing LLD participant data point due to researcher omission) (trait anxiety  $t=8.68$ ,  $df=35$ ,  $p<0.001$ ; one missing LLD participant data point due to researcher omission; state anxiety pre-test  $t=8.99$ ,  $df=36$ ,  $p<0.001$ )

(Table 2)

### Facial Expression Recognition Task (FERT)

Neither accuracy nor misclassifications varied between groups either across all emotional valences or by emotional valence. However, for reaction times there was a significant interaction between group

and valence ( $F(3,90)=3.94, p=0.011$ ) in this task. Post hoc tests indicated that LLD participants were significantly slower than controls when identifying surprised faces ( $t(1,35)=2.85, p=0.007$ ), with no other significant group differences on reaction times for other valences (see Figure 2, panel a).

#### Facial Dot Probe Task (FDOT)

There was a significant main effect of congruency ( $F(1,31)= 5.74, p=0.023$ ) indicating that all participants showed a general bias away from emotional faces. There was no main effect of masking, valence, or group, and no interactions within group and masking, valence or congruency (all  $p$  values  $>0.05$ ) (see figure 2 panel d).

#### Emotion Word Categorisation and Recall (ECAT and EREC)

There were no significant group differences in accuracy ( $f(1,32)=2.205, p=1.47$ ) or reaction time ( $f(1,32)=2.484, p=0.125$ ) on the ECAT. On the EREC, depressed participants recalled significantly fewer words than controls ( $f(1,32)=6.475, p=0.016$ ), with no difference in this effect between positive and negative words ( $f(1,32)=0.449, p=0.508$ ) (see Figure 2, Panel b). There was no significant effect of group on misremembered adjectives ( $f(1,32)=0.127, p=0.725$ ).

#### Scrambled Sentences Task

Negativity scores from the scrambled sentence task (i.e. proportion of trials in which participants solved the task by generating a negative sentence) were significantly higher in depressed participants than in controls ( $F(1,30)=13.4, p=0.001$ ) (see Figure 2, panel c).

#### Post-hoc correlation

In order to assess whether the various cognitive measures that differed between groups were manifestations of a general underlying negative bias, correlations between the negativity score in the scrambled sentences task, reaction times to surprised faces in the FERT, and recall of adjectives in EREC were assessed specifically within the LLD group. No significant correlations were found ( $r=0.448, p=0.06$  to  $r=-0.21, p=0.38$ ).

#### Sensitivity analysis excluding LLD participants on sedating medication

As 7 participants in the LLD group were receiving sedating medications which can impact on cognitive function, a sensitivity analysis was performed having excluded these participants. There was now no significant difference between MOCA scores of LLD participants compared to controls ( $t(1,28)=-1.178; p=0.248$ ). FERT and interpretation results remained the same. In the recall task there was no main effect of MOCA but other effects persisted. In the attention task there was now an



interaction between masking and group, both groups were slower for unmasked faces compared to masked faces, and this increase in reaction times was more pronounced for depressed participants than controls ( $f(1,24)=5.04, p=0.034$ ).

Effects of baseline cognitive function are reported in the Appendix.

## Discussion

The aim of the current study was to investigate whether negative cognitive bias is present in late life depression using a range of measures across different cognitive domains. We found evidence for negative cognitive bias in interpretation. There was no evidence of negative bias in attention or memory; however, participants with LLD were slower to recognise surprised faces, and performed overall more poorly on the memory task.

In terms of interpretation, LLD participants showed a negative cognitive bias and were more likely than controls to create negative statements in the scrambled sentence task. It might be argued that this difference could reflect a positive interpretation bias in controls. However, the negativity scores in the control group are broadly consistent with control groups in studies of adults of working age<sup>33, 34, 35</sup>. Although interpretation bias has not been investigated in LLD before, there is evidence of this bias in adults of working age<sup>12, 13, 33</sup> and evidence that cognitive bias modification of interpretation (CBM-I) can improve mood<sup>36-38</sup>. It has been suggested that negative interpretation bias is due to underlying negative core beliefs<sup>39</sup> which drive a number of cognitive processes. For example, negative memories may guide attention to negative stimuli in the environment, resulting in increased stress levels and negative interpretations<sup>40</sup>. It is interesting, however, that in the current study there is evidence for a negative interpretation bias in the absence of a bias in memory or attention. Other models suggest negative interpretations stimulate negative images<sup>41</sup> or cognitions<sup>42</sup> which in turn result in increased negative mood and further negative interpretations.

LLD participants were significantly slower than controls to identify surprised faces. Surprised facial expressions are sometimes conceptualised as being relatively positive in nature<sup>43, 44</sup>. Participants in the LLD group may have slower cognitive processing of, and difficulty making decisions about, positive expressions relative to negative expressions<sup>16</sup>. Against this hypothesis, no difference in reaction times to happy faces was observed and the overall pattern of facial expression recognition across different emotions and outcome measures did not suggest a negative bias. Alternatively,

surprised expressions have been described by some authors as ambiguous<sup>45</sup>, or transitory<sup>11</sup>, and the longer reaction times seen in LLD participants may reflect a difficulty in interpreting these more ambiguous facial expressions. This finding contrasts with previous studies of facial expression recognition in older adults, where no studies have reported differences in reaction times, although others have reported bias in accuracy<sup>16, 18, 19</sup>.

On the memory task (EREC) LLD participants showed a worse performance in recall of adjectives. While LLD participants also had significantly lower MOCA scores than controls, the difference in performance on EREC persisted when MOCA score was included as a covariate in the analysis. Other studies have shown that people with depression perform more poorly on recall tasks<sup>4,5,46,47</sup>. It has been suggested that this may be due to deficits in retrieval and this in turn is due to impaired executive function, and difficulty generating strategies to initiate retrieval<sup>5, 46,47</sup>. There was no negative bias in recall or in categorisation of valence of adjectives. Previous studies of LLD have shown bias in recognition<sup>15</sup> and immediate recall<sup>4,5</sup> but, similarly to the findings of this study, this bias is not sustained after a delay<sup>5</sup>.

The lack of evidence for a negative bias in attention and memory in this study contrasts with some previous findings in LLD<sup>4-7,14</sup> and with studies investigating younger adults with depression<sup>8-11</sup>, where these biases have been described. All but one of the LLD participants in the current study were taking anti-depressant medication. Studies in younger adults have shown that negative cognitive bias is reduced by anti-depressant medication<sup>31</sup>. Furthermore, Shiroma et al (2014)<sup>17</sup> showed in older adults that accuracy of recognition of positive facial expressions improved with anti-depressant treatment. It is therefore possible that anti-depressant medication may have reduced negative biases in attention, memory and emotional expression recognition in this study. Alternative possibilities are that differences in the exact nature of the cognitive tasks used, or the populations recruited have resulted in differing findings. Lastly, it may be that older adults with depression do not show the same global pattern of negative bias seen in adults of working age, and that there is a difference in the nature of cognition in depression in older adults. Indeed, it has been suggested that older adults with depression tend to emphasise somatic rather than cognitive symptoms<sup>48</sup> and that LLD may result in reduced reactivity to and altered experience of emotional stimuli rather than negative biases<sup>3</sup>.

There are a number of limitations to this study. The sample size is small, although it is comparable to the majority of other studies in this area, reflecting the challenges of recruitment in this highly

morbid population. Larger representative samples are required in future studies. The MOCA scores in the LLD group were significantly lower than the control group, and seven LLD participants were taking sedating medications. MOCA score, age, gender and years of education were therefore included as covariates in the analyses and in addition a sensitivity analysis was performed which excluded the LLD participants taking sedating medications. The differences in interpretation, recall and expression recognition all persisted when these participants were excluded, suggesting that these group difference do not account for the observed effects. A study strength is that it is the first time one study has examined multiple cognitive domains in LLD. In addition there is a high level of morbidity in the LLD group which may increase the generalisability of the findings to real world clinical populations.

This study provides new evidence of negative bias in interpretation in older adults with depression, but did not show a global bias across cognitive domains. These findings may be relevant to patients in primary and secondary care suffering from depression, including inpatients and those presenting a high level of risk. Further work is needed to define the nature of cognitive bias in older adults with depression and to explore the feasibility and efficacy of CBM-I in this population. The development of non-pharmacological approaches to depression have the great advantage of reducing poly-pharmacy and side effects, and could be very beneficial for older people with depression.

In summary, this study has identified a negative bias in interpretation in people with LLD. It would be useful for future studies to test the clinical impact of interventions designed to target these biases.

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## Tables

**Table 1: Demographic characteristics and baseline subjective mood (means and standard deviations)**

	Late Life Depression Group	Control Group
N	19	19
Gender (male: female)	9:10	9:10
Years of education (<12:>12)	4:15	4:15
Age	70 (8.17)	71 (7.95)
MOCA score	25 (3.14)	27 (2.60)
NART score	126 (2.22)	127 (1.62)
HDRS score <sup>†</sup>	21(4.41)	1 (0.23)
Trait anxiety <sup>† ‡</sup>	56 (11.81)	28 (6.57)
State anxiety <sup>‡</sup>	49 (10.96)	25 (4.12)

<sup>†</sup>1 missing data point, LLD group <sup>‡</sup>assessed using STAI

**Table 2: Clinical characteristics of depressed participant group (numbers of participants)**

N	19
Taking one antidepressant only	9
Taking combination of two antidepressants	4
Taking combination of 1 or 2 antidepressants and lithium	2
Taking combination of 1 or 2 antidepressants and an antipsychotic	6
Taking hypnotic medication	6
Depression specifier as identified on the MINI:	
<i>Melancholic features</i>	12
<i>Recurrent depression</i>	12
<i>Risk of suicide</i>	3

## Figure Legends

Figure 1: Flow chart to show number of people screened, number not eligible, number declined, and number of participants, LLD and controls



Figure 2. Panel A: reaction times to identify facial expressions in the FERT for LLD participants and controls. (reaction times for surprise were significantly longer in LLD than controls). Panel B: number of positive and negative adjectives recalled in the EREC by LLD participants and controls (the number of adjectives recalled (positive and negative) were significantly lower for LLD than controls). Panel C: negativity scores on the scrambled sentences task, LLD participants and controls (negativity scores were significantly higher in LLD than controls). Panel D: vigilance scores in the FDOT for LLD participants and controls. Vigilance was calculated as the reaction time difference between incongruent and congruent trials (there were no significant differences in vigilance scores of LLD participants compared to controls). All graphs display mean scores with error bars reporting standard error. Dark grey bars represent control participants and pale grey bars represent LLD participants. For significant comparisons \* $p < 0.05$ .