Behavioral and neuroimaging evidence prodromal to major depressive disorder onset in a young adult without personal or family history of psychiatric disorder: Case report

Rachel Miceli[1],

Skye Satz[1],

Holly A. Swartz,

Anna Manelis[*]

Department of Psychiatry, Western Psychiatric Institute and Clinic, University of Pittsburgh Medical Center, University of Pittsburgh, 230 McKee Pl, Room 226, Pittsburgh, PA 15213, USA

Abstract

Background: Subthreshold symptoms of major depressive disorder (MDD) may be underreported due to stigma and/or cognitive impairment associated with this illness. Identifying objective behavioral and neural markers prodromal to MDD onset would help overcome this bias. This case study reports prospective behavioral and neuroimaging evidence prodromal to MDD onset in a young adult without prior personal or family history of psychiatric disorders who was identified during a longitudinal study of mood disorders.

Methods: The participant completed the SCID-5 and other assessments of depression as well as the Vividness of Visual Imagery Questionnaire at baseline, 6-month follow-up, and 12-month follow-up. The participant completed the Emotion Intensity Rating task and high-resolution structural images were collected using magnetic resonance imaging (MRI) at baseline and 6-month follow-up. The levels of cortical myelin computed as the T1w/T2w ratio were used in a linear discriminant analysis (LDA) to predict participant's diagnostic status at baseline and 6-months.

Results: The participant presented as a healthy control at baseline and 6-month but met criteria for MDD at the 12-month follow-up based on the SCID-5. The participant's visual imagery as well as the ability to correctly recognize neutral faces dramatically reduced from baseline to 6-month follow-up. The LDA classified the participant as an individual with depressive disorders at both baseline and 6-month follow-up despite the absence of either subthreshold or clinical symptoms of depression.

Conclusions: While preliminary, the results suggest that the measures of cortical myelin, response to neutral and emotional facial expressions, and vividness of visual imagery could be

[*]Corresponding author. anna.manelis@gmail.com (A. ManSSSelis).
[1]These authors equally contributed to this work.

prodromal to illness onset, whereas clinician-administered or self-reported measures of depression symptoms were uninformative.

Keywords

Major depressive disorder; Depression; Cortical myelin; Facial expressions; Emotion intensity ratings; Vividness of visual imagery

1. Introduction

Major depressive disorder (MDD) is a debilitating mental illness characterized by episodes of feeling down, sad, hopeless, worthless, fatigued, having low interest in previously enjoyable activities, and experiencing alterations in sleeping, eating, and overall cognitive and psychosocial functioning (First et al., 2015; Judd et al., 2000). Understanding prodromal symptomatology predicting major depressive disorder is critically important because this may help improve long-term outcomes and decrease the burden of this disorder on mental health care system and society in general (Kakuma et al., 2011; Mendelson and Tandon, 2016).

Currently, the mental health field relies on information reported by patients to identify depressive symptoms and diagnose mental illness. Prodromal symptoms of depression are often identified retrospectively based on the patient or their significant others' reports or on the existing medical records (Benasi et al., 2021). However, patients may underreport subthreshold symptoms of depression due to stigma associated with this illness or cognitive impairment associated with depression thus affecting the clinician's ability to diagnose the disorder and offer treatment options in a timely manner (Henshaw, 2014). Identifying objective behavioral and neural correlates prodromal to depression onset would help overcome symptom self-report bias.

The participant discussed here was enrolled in an ongoing longitudinal neuroimaging study of mood disorders. The participant entered the study as a healthy control and remained healthy at the 6-month follow-up. The participant met criteria for MDD during the 12-month follow-up. The data collected over the three time points offered us the convenience of observing clinical, behavioral, and neural changes associated with illness transition in real time. Considering that observing the onset of MDD within the course of a study is rare, reporting such cases is critically important to help understand the possible prodromal markers of MDD in previously healthy individuals. The information regarding prodromal markers of MDD may inform the staging model of psychiatric disorders (McGorry et al., 2014) and provide an opportunity for developing therapeutic interventions before acute symptoms and a decrease in quality of life occur.

2. Methods

2.1. Participants

This study was approved by the University of Pittsburgh Institutional Review Board. All participants gave their written informed consent to participate in the study, were right-handed, fluent in English, and were matched on age and sex. Individuals with depressive

disorders (DD) met DSM-5 criteria for major or persistent depressive disorders. Healthy controls (HC) had no personal or family history of psychiatric disorders. The data for the participant discussed in this case study were compared with the data collected from 18–45-year-old individuals who participated in the same longitudinal study and consisted of 47 HC and 39 individuals with DD. The findings associated with this sample were previously published by our lab (Baranger et al., 2021b, 2021a).

Although this report is based on a real case, all identifying information for the individual has been altered to protect patient confidentiality. A male Caucasian participant between 25–30 years of age with normal level of intelligence (IQ>100 on the NART assessment (Nelson, 1982)) and college-level education participated in three clinical study visits (at baseline 6-month follow-up, and 12-month follow-up) and in two behavioral/neuroimaging appointments (at baseline and 6-month follow-up). Based on the SCID-5 assessment, the participant presented as a healthy control without reported trauma, substance abuse, medical conditions or family or personal history of psychiatric disorders, at baseline and 6-month follow-up. However, the participant met DSM-5 criteria for Major Depressive Disorder, Single Episode, In Full Remission (F32.5) at 12-month follow-up and reportedly began to receive regular individual counseling sessions and Wellbutrin 300 mg daily approximately 5-months prior to his 12-month follow-up.

2.2. Clinical assessment

The participant's diagnostic status was determined at each time point using Structured Clinical Interview for DSM-5 (SCID-5) (First et al., 2015). Current symptoms of depression were assessed using the standard Hamilton Rating Scale of Depression (HRSD-25 (Hamilton, 1960)). Both assessments were administered by a Master-level clinician trained in psychiatric assessments. The Functioning Assessment Short Test (FAST (Rosa et al., 2007)) was used to assess difficulties in functioning: autonomy, occupational functioning, cognitive functioning, financial issues, interpersonal relationships, and leisure time. In addition, the Quick Inventory of Depressive Symptomatology-Self-Report version (QIDS-SR (Rush et al., 2003)) was administered to obtain additional information the additional information about current symptoms of depression as well as the MOODS-SR questionnaire (Dell'Osso et al., 2002) depression scale to obtain the information about lifetime symptoms of depression prior to baseline, at baseline, between baseline and 6-months follow-up, at 6-months follow up, between 6-months and 12-months follow-ups, and at 12-months follow-up. The Snaith-Hamilton Pleasure Scale (SHAPS (Snaith et al., 1995)) measured feelings of anhedonia. Spielberger's State-Trait Anxiety Inventory (STAIY (Spielberger et al., 1983)) was used to evaluate state anxiety (STAIY1) and trait anxiety (STAIY2). Previous studies suggest that anxiety and anhedonia are common prodromal clinical symptoms of depression (Benasi et al., 2021). For all assessments described above, higher scores indicate more severe symptoms of psychopathology.

In addition, we have administered the Vividness of Visual Imagery Questionnaire (VVIQ (Marks, 1973)) to assess the participants' vividness of visual imagery at each time point. The VVIQ provides participants with prompts (e.g., "Think of some relative or friend whom you frequently see (but who is not with you at present), and carefully consider the picture

that comes before your mind's eye") and asks to imagine the scene described in each prompt (e.g., "the exact contour of face, head, shoulders, and body"). The participant rates the clarity of the scenes they imagined on a scale from 1 ("perfectly clear and as vivid as normal vision") to 5 ("no image at all (only "knowing" that you are thinking of the object)). Higher scores indicate less vivid visual imagery. Vividness of visual imagery is a construct referring to clarity, richness, and detail of an image compared to an actual percept (D'Angiulli and Reeves, 2007). Previous studies suggested that symptoms of depression affect visual imagery (Weßlau et al., 2015).

2.3. Behavioral task

The participant performed the Emotion Intensity Rating task (Manelis et al., 2019) during which he encountered a total of 96 pictures of happy (n=32), sad (n=32), and neutral (n=32) faces of men and women presented one at a time. Each face was shown in the center of the computer screen and had to be rated on a scale from 1–9 that was shown under the image of the face. The faces perceived as sad had to be rated from 1 (very sad) to 4 (a little sad), neutral faces had to be rated as 5, and happy faces had to be rated from 6 (a little happy) to 9 (very happy). The participant was instructed that there was no right or wrong answer and that the judgments regarding emotional intensity of each face should be made based on participant's personal perception of each facial expression.

2.4. Neuroimaging data acquisition

High-resolution T1w (TR=2400ms, $0.8 \times 0.8 \times 0.8mm^3$, 208 slices, FOV=256, TE=2.22ms, flip angle=8°) and T2w images (TR=3200ms, $0.8 \times 0.8 \times 0.8mm^3$, 208 slices, FOV=256, TE=563ms) as well as the spin echo images (TR=8000, $2 \times 2 \times 2mm^3$, FOV=210, TE=66ms, flip angle=90°, 72 slices) were collected at the University of Pittsburgh/UPMC Magnetic Resonance Research Center using a 3T Siemens Prisma scanner with a 64-channel receiver head coil. The same set of images was collected at baseline and 6-month follow-up. The DICOM images were converted to BIDS dataset using *heudiconv* (Halchenko et al., 2019) and *dcm2niix* (Li et al., 2016).

2.5. Data analyses

2.5.1. Emotion intensity rating task—In the Emotion Intensity Rating task, we computed the participant's accuracy by calculating a percent of correctly identified facial expressions (e.g., happy face is identified as happy) for each emotional condition (i.e., happy, neutral, and sad) at baseline and 6 months. The accuracy calculation did not take into account the intensity ratings. For example, all happy faces rated between 6 and 9 were correct responses. In addition, we used a paired t-test to compare emotional intensity ratings for 32 trials of sad, neutral, and happy facial expressions (analyzed separately) at baseline vs. 6 months. This test included all trials in a specific emotional condition independently of the response accuracy.

2.5.2. Neuroimaging—The details of the neuroimaging data preprocessing and analysis have been reported previously (Baranger et al., 2021b, 2021a) and are publicly available at https://github.com/manelis-lab/myelin-paper-NICL2021. In short, we employed the HCP pipeline to preprocess T1w and T2w images and to compute the T1w/T2w ratio that is

thought to reflect the levels of cortical myelin (Glasser et al., 2013, 2016; Glasser and van Essen, 2011). Spin echo field maps were used for bias field correction. The myelin maps were parcellated into 360 parcels (Glasser et al., 2016) and the mean T1w/T2w ratio was computed for each parcel. For the sample of 47 HC and 39 individuals with DD, only structural images collected at baseline were used. For the participant described in this case report, both the images collected at baseline and those collected at 6-months were computed. The elastic net regularized regression (Zou and Hastie, 2005; Friedman et al., 2010) was employed in the sample of 47 HC and 39 individuals with DD to identify parcels that were most predictive of HC vs. DD status. This sample did not include the participant who we discuss in the case study. The elastic net regularized regression revealed that 33 out of 360 parcels were most informative to discriminate between HC vs. DD. These parcels were located in the orbitofrontal cortex, insula, cingulate, frontal operculum, auditory and visual cortices. After that, the mean values of the T1w/T2w ratio in these 33 parcels were used as inputs to a linear discriminant analysis (LDA) (Venables and Ripley, 2002) to classify HC vs. DD in the same sample of individuals using a leave-one-out cross-validation procedure. After we found that the model classified these two groups with 68% of accuracy (Baranger et al., 2021b, 2021a), we examined whether the values of cortical myelin in the 33 parcels described above would classify the participant of interest as a HC or as an individual with DD at baseline and at 6-month when no symptoms of depression were yet reported. To achieve this goal, we trained the LDA on the full sample of 47 HC vs.39 DD, and then tested the model on the participant described in this case report to predict his diagnostic status at baseline and then at 6-months (Baranger et al., 2021b, 2021a).

3. Results

3.1. Clinical

During the baseline and 6-month follow-up, the participant did not meet criteria for any DSM-5 diagnosis nor reported any depressive symptomology on the SCID-5. At the 12-month follow-up, the participant disclosed that he had experienced a month-long episode of depression with onset approximately one month after his 6-month follow-up study visit. During that episode he felt down and sad, lost interest in previously pleasurable activities (e.g., physical exercising), felt fatigued and guilty, had difficulty concentrating and focusing, and slept longer than usual (up to 10 h). The participant also reported isolating from others, having a decrease in quality of his work and an increase in his substance use (i.e., alcohol and cannabis). The participant sought help from a therapist who diagnosed him with MDD and Generalized Anxiety Disorder (GAD). A month later, the participant's diagnosis was confirmed by a psychiatrist who prescribed him Wellbutrin 300mg daily. Consistent with this finding, the participant met criteria for Major Depressive Disorder, Single Episode, Full Remission (F32.5) during the 12-month follow-up study visit. The results for the other assessments are presented in Table 1 and on Fig. 1.

3.2. Behavioral

Fig. 2 illustrates the mean recognition accuracy for sad, neutral, and happy facial expressions at baseline and 6-month follow-up. It appears that the participant's ability to recognize happy and sad facial expressions was extremely high during both baseline and

6-month follow-up (100% accuracy for happy and sad faces at baseline, 93.75% and 96.88% accuracy for happy and sad faces accordingly at 6-month follow-up). However, his ability to recognize neutral facial expressions as neutral dramatically reduced from 93% at baseline to 6.25% at 6-month follow-up (Fig. 2). The paired t-tests showed that the mean ratings for emotion intensity of facial expressions also significantly changed over time. Compared to baseline, the ratings made during the 6-month follow-up study visit became less negative for sad faces (t(31)= −5.8, p<0.001), less positive for happy faces (t(31)=5.7, p<0.001), and more negative for neutral faces (t(31)=2.6, p=0.014) (Fig. 3).

3.3. Neuroimaging

As described in our previous publications, the LDA model classified the participant we discuss here as an individual diagnosed with DD during both baseline and 6-month follow-up scans despite the lack of subthreshold or clinical symptoms of depression (Baranger et al., 2021b, 2021a).

4. Discussion

In this case report, we described the prospective clinical, behavioral, and neuroimaging measures prodromal to onset of MDD. Our results suggest that most available clinical measures remained at the normal level a month before illness onset and were unable to predict upcoming symptoms of depression. At the 12-month follow-up study visit, after onset of MDD, the participant showed a slight increase in depression based on the HRSD-25 assessment, however, the score "7" was still within the normal range. The participant also showed a minimal increase in self-reported symptoms of depression between the 6-month and 12-month follow-ups based on the MOODS-SR scores, but the score "2" on the MOODS-SR depression scale is consistent with the mean score observed by Baranger et al., (2021b) in healthy individuals (mean[SD]=2.15[2.27]) rather than individuals diagnosed with depressive disorders (mean[SD]=18.41[4.36]). These relatively low scores for depression symptoms at the 12-month follow-up corresponded to the participant being in full remission from the previously experienced major depressive episode 5 months prior. A nominal increase in past and current symptoms of depression toward 12-month follow-up was paralleled by an increase in trait anxiety with about 15-point change from baseline to 12-month follow-up. Trait anxiety refers to the stable inclination to experience anxiety and fear and to perceive environment as threatening (Spielberger et al., 1983). Therefore, the changes in trait anxiety without changes in state anxiety may show that the participant started to exhibit more persistent anxiety symptoms and may indicate the alteration in stable representation of self and environment that preceded onset of MDD. These findings are consistent with a recent systematic review implicating anxiety as one of the prodromal symptoms of depression onset (Benasi et al., 2021).

Considering that subthreshold symptoms of depression may be unrecognized or underreported by patients (Henshaw, 2014), we examined the potential of behavioral and neural measures to predict illness onset. Altered level of cortical myelin was the earliest sign of illness before the participant met criteria for depressive disorders diagnosis. Myelin levels were consistent with those observed in individuals with depressive disorders rather

than healthy controls during both baseline and 6-months appointments (Baranger et al., 2021b). This finding suggests that disrupted levels of myelin might be an early biological risk marker specific to MDD or common across various mental illnesses (McTeague et al., 2017). We should note that one limitation of the machine learning analysis was a relatively small training sample (47 HC vs. 39 DD). Although it could be argued that this sample may not be representative in the high-dimensional space of 360 parcels, the elastic net showed a robust performance when the number of predictors is larger than the number of observations (Zou and Hastie, 2005, Friedman et al., 2010) and was successfully used with neuroimaging data (Jollans et al., 2019).

Other early indicators of changing mental health included reduced recognition accuracy for neutral facial expressions and lower intensity ratings for sad, neutral, and happy faces observed prior to illness onset. The reduced accuracy results were congruent with our previous findings (Manelis et al., 2019). However, the reduction in the recognition accuracy for neutral faces from 93% at baseline to 6.25% at the 6-month follow-up was much more pronounced than differences between healthy individuals and currently depressed individuals (90% vs. 70% accordingly) observed in Manelis et al. (2019). In addition to misjudging neutral faces as emotional (mostly sad), the participant's ratings of happy and sad faces became lower with happy faces judged as less happy and sad faces judged as less sad closer to illness onset at 6-month follow-up. These findings are consistent with previous reports of blunted emotional response (Rottenberg and Hindash, 2015) and negative bias to future emotional experiences (Strunk and Adler, 2009; Andersen et al., 1992) in people with depression.

It is interesting that depression onset was preceded not only by alterations in the levels of cortical myelin and responses to neutral and emotional stimuli, but also by a decrease in vividness of visual imagery that was especially pronounced between baseline and 6-month follow-up. This result extends the previously observed relationship between imagery and depression (Weßlau et al., 2015) and suggests that the decrease in vividness of visual imagery may precede symptoms of depression.

In summary, this case report presented clinical, behavioral, and neuroimaging evidence associated with onset of MDD in a young adult without prior family or personal history of psychiatric disorders. It appears that the measures of cortical myelin, response to neutral and emotional facial expression, and vividness of visual imagery were prodromal to illness onset, whereas clinician-administered or self-reported measures of depression symptoms were uninformative even after the official diagnosis was established by a therapist, a psychiatrist, and a study clinician.

## Acknowledgments

Data availability

Patient data supporting the results described in this case report can be obtained from the corresponding author upon a reasonable request.

References

Andersen SM, Spielman LA, Bargh JA, 1992. Future-event schemas and certainty about the future: automaticity in depressives' future-event predictions. J. Pers. Soc. Psychol 63, 711–723. [PubMed: 1447691]

Baranger DAA, Halchenko YO, Satz S, Ragozzino R, Iyengar S, Swartz HA, et al. , 2021a. Protocol for a machine learning algorithm predicting depressive disorders using the T1w/T2w ratio. MethodsX 8, 101595. doi:10.1016/j.mex.2021.101595. [PubMed: 35004227]

Baranger DAA, Halchenko YO, Satz S, Ragozzino R, Iyengar S, Swartz HA, et al. , 2021b. Aberrant levels of cortical myelin distinguish individuals with depressive disorders from healthy controls. NeuroImage Clin 32, 102790. doi:10.1016/j.nicl.2021.102790. [PubMed: 34455188]

Benasi G, Fava GA, Guidi J, 2021. Prodromal symptoms in depression: a systematic review. Psychother. Psychosom 90, 365–372. doi:10.1159/000517953. [PubMed: 34350890]

D'Angiulli A, Reeves A, 2007. The relationship between self-reported vividness and latency during mental size scaling of everyday items: phenomenological evidence of different types of imagery. Am. J. Psychol 120, 521–551. [PubMed: 18277515]

First MB, Williams JBW, Karg RS, Spitzer RL, 2015 Structured clinical interview for DSM-5— research version (SCID-5 for DSM-5, research version; SCID-5-RV)

Dell'Osso L, Armani A, Rucci P, Frank E, Fagiolini A, Corretti G, et al. , 2002. Measuring mood spectrum: comparison of interview (SCI-MOODS) and self-report (MOODS-SR) instruments. Compr. Psychiatry 43, 69–73. doi:10.1053/comp.2002.29852. [PubMed: 11788923]

Friedman J, Hastie T, Tibshirani R, 2010. Regularization paths for generalized linear models via coordinate descent. J. Stat. Softw 33, 1–22. doi:10.18637/jss.v033.i01. [PubMed: 20808728]

Glasser MF, Coalson TS, Robinson EC, Hacker CD, Harwell J, Yacoub E, et al. , 2016. A multi-modal parcellation of human cerebral cortex. Nature 536, 171–178. doi:10.1038/nature18933. [PubMed: 27437579]

Glasser MF, Sotiropoulos SN, Wilson JA, Coalson TS, Fischl B, Andersson JL, et al. , 2013. The minimal preprocessing pipelines for the human connectome project. Neuroimage 80, 105–124. doi:10.1016/j.neuroimage.2013.04.127. [PubMed: 23668970]

Glasser MF, van Essen DC, 2011. Mapping human cortical areas in vivo based on myelin content as revealed by T1- and T2-weighted MRI. J. Neurosci 31, 11597–11616. doi:10.1523/JNEUROSCI.2180-11.2011. [PubMed: 21832190]

Halchenko Y, Goncalves M, Castello MV di O, Ghosh S, Hanke M, Dae, et al. nipy/heudiconv: v0.5.4 [0.5.4] - 2019–04-29 2019. 10.5281/ZENODO.2653784.

Hamilton M, 1960. A rating scale for depression. J. Neurol. Neurosurg. Psychiatry 23, 56–62. doi:10.1136/jnnp.23.1.56. [PubMed: 14399272]

Henshaw EJ, 2014. Too sick, not sick enough? Effects of treatment type and timing on depression stigma. J. Nerv. Ment. Dis 202, 292–299. doi:10.1097/NMD.0000000000000121. [PubMed: 24647215]

Jollans L, Boyle R, Artiges E, Banaschewski T, Desrivières S, Grigis A, et al. , 2019. Quantifying performance of machine learning methods for neuroimaging data. Neuroimage 199, 351–365. doi:10.1016/j.neuroimage.2019.05.082. [PubMed: 31173905]

Judd LL, Akiskal HS, Zeller PJ, Paulus M, Leon AC, Maser JD, et al. , 2000. Psychosocial disability during the long-term course of unipolar major depressive disorder. Arch. Gen. Psychiatry 57, 375–380. [PubMed: 10768699]

Kakuma R, Minas H, Van Ginneken N, Dal Poz MR, Desiraju K, Morris JE, et al. , 2011. Human resources for mental health care: current situation and strategies for action. Lancet 378, 1654–1663. doi:10.1016/S0140-6736(11)61093-3. [PubMed: 22008420]

Li X, Morgan PS, Ashburner J, Smith J, Rorden C, 2016. The first step for neuroimaging data analysis: DICOM to NIfTI conversion. J. Neurosci. Methods 264, 47–56. doi:10.1016/j.jneumeth.2016.03.001. [PubMed: 26945974]

Manelis A, Huppert TJ, Rodgers E, Swartz HA, Phillips ML, 2019. The role of the right prefrontal cortex in recognition of facial emotional expressions in depressed individuals: fNIRS study. J. Affect. Disord 258, 47–56. doi:10.1016/j.jad.2019.08.006.

Marks DF, 1973. Visual imagery differences in the recall of pictures. Br. J. Psychol 64, 17–24. [PubMed: 4742442]

McGorry P, Keshavan M, Goldstone S, Amminger P, Allott K, Berk M, et al. , 2014. Biomarkers and clinical staging in psychiatry. World Psychiatry 13, 211–223. doi:10.1002/wps.20144. [PubMed: 25273285]

McTeague LM, Huemer J, Carreon DM, Jiang Y, Eickhoff SB, Etkin A, 2017. Identification of common neural circuit disruptions in cognitive control across psychiatric disorders. Am. J. Psychiatry 174, 676–685. doi:10.1176/appi.ajp.2017.16040400. [PubMed: 28320224]

Mendelson T, Tandon SD, 2016. Prevention of depression in childhood and adolescence. Child Adolesc. Psychiatr. Clin. N. Am 25, 201–218. doi:10.1016/j.chc.2015.11.005. [PubMed: 26980124]

Nelson HE, 1982. National adult reading test (NART): test manual. Wind UK NFER-Nelson 124, 0–25.

Rosa AR, Sánchez-Moreno J, Martínez-Aran A, Salamero M, Torrent C, Reinares M, et al. , 2007. Validity and reliability of the functioning assessment short test (FAST) in bipolar disorder. Clin. Pract. Epidemiol. Ment. Health 3, 1–8. doi:10.1186/1745-0179-3-5. [PubMed: 17274830]

Rottenberg J, Hindash AC, 2015. Emerging evidence for emotion context insensitivity in depression. Curr. Opin. Psychol 4, 1–5. doi:10.1016/j.copsyc.2014.12.025.

Rush AJ, Trivedi MH, Ibrahim HM, Carmody TJ, Arnow B, Klein DN, et al. , 2003. The 16-item quick inventory of depressive symptomatology (QIDS), clinician rating (QIDS-C), and self-report (QIDS-SR): a psychometric evaluation in patients with chronic major depression. Biol. Psychiatry 54, 573–583. doi:10.1016/S0006-3223(02)01866-8. [PubMed: 12946886]

Snaith RP, Hamilton M, Morley S, Humayan A, Hargreaves D, Trigwell P, 1995. A scale for the assessment of hedonic tone the Snaith-Hamilton Pleasure Scale. Br. J. Psychiatry 167, 99–103. [PubMed: 7551619]

Spielberger CD, Gorsuch RL, Lushene R, Vagg PR, Jacobs GA, 1983. Manual for the State-Trait Anxiety Inventory. Manual for the State-Trait Anxiety Inventory Consulting Psychologists Press, Inc., Palo Alto, CA.

Strunk DR, Adler AD, 2009. Cognitive biases in three prediction tasks: a test of the cognitive model of depression. Behav. Res. Ther 47, 34–40. doi:10.1016/j.brat.2008.10.008. [PubMed: 19010460]

Venables WN, Ripley BD, 2002. Modern Applied Statistics with S. Fourth edi. Modern Applied Statistics with S. Fourth Edition Springer.

Weßlau C, Cloos M, Höfling V, Steil R, 2015. Visual mental imagery and symptoms of depression - results from a large-scale web-based study. BMC Psychiatry 15, 308. doi:10.1186/s12888-015-0689-1. [PubMed: 26631081]

Zou H, Hastie T, 2005. Regularization and variable selection via the elastic net. J. R. Stat. Soc. Ser. B Stat. Methodol 67, 301–320. doi:10.1111/j.1467-9868.2005.00503.x.
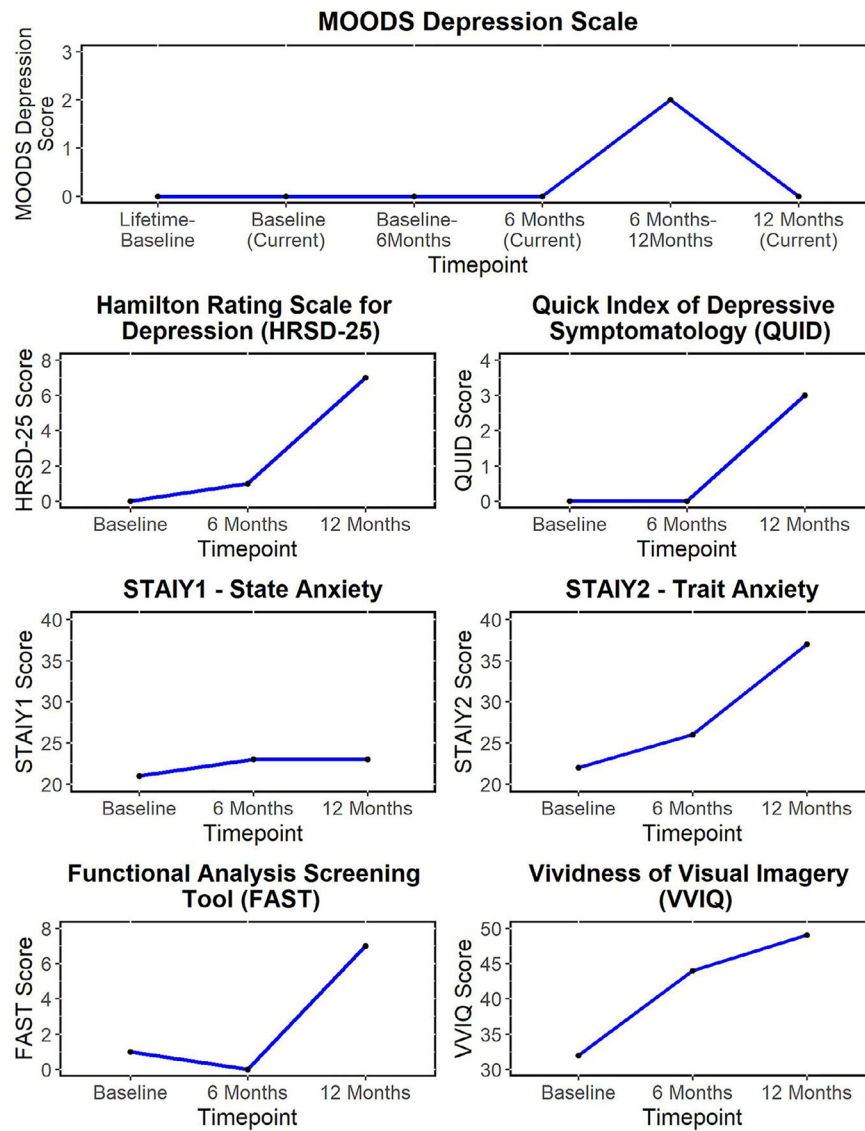
Fig. 1.
Longitudinal changes in clinical assessments and VVIQ.
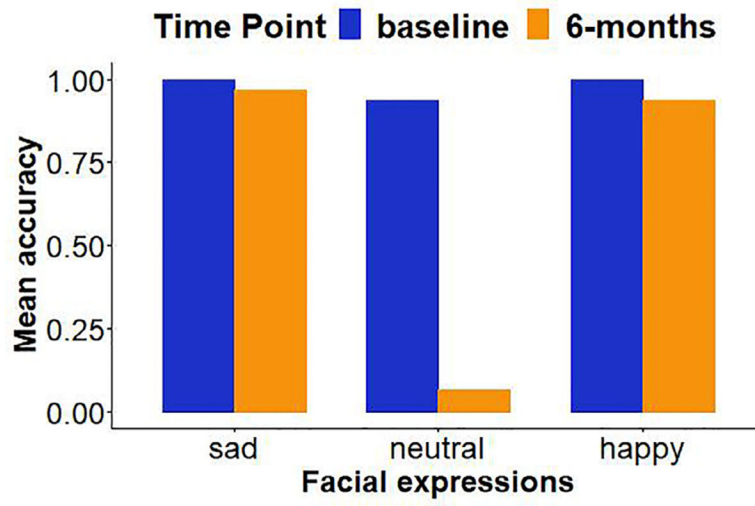
Fig. 2.
Mean accuracy for recognition of sad, neutral, and happy emotional expressions at baseline and 6-month follow-up.
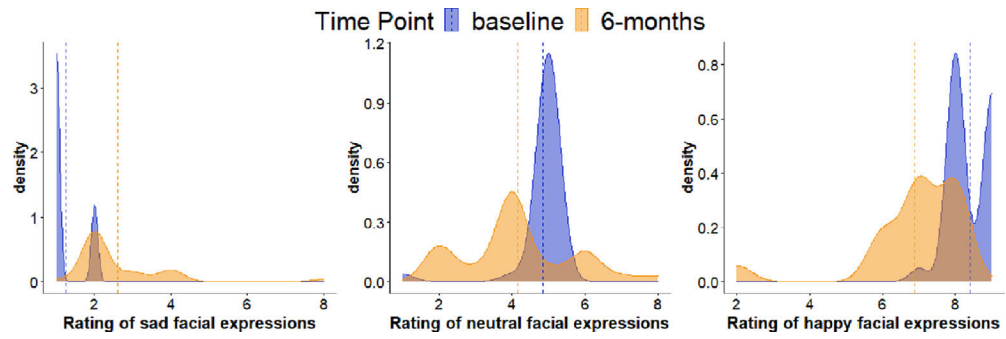
Fig. 3.
Density distribution for sad, neutral, and happy face ratings at baseline and 6-month follow-up. The vertical dashed lines illustrate mean ratings for each emotion at each time point.

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

Table 1

Longitudinal changes in clinical assessments and VVIQ.

Assessment	Lifetime prior baseline	Baseline	Baseline to 6-months	6-months	6-months to 12-months	12-months	Range of scores	Notes
HRSD-25	na	0	na	1	na	7	0–72	Higher score corresponds to more severe symptoms
FAST	na	1	na	0	na	7	0–72	
MOODS-SR depression scale	0	0	0	0	2	0	0–22	
QIDS-SR	na	0	na	0	na	3	0–27	
STAIY1	na	21	na	23	na	23	20–80	
STAIY2	na	22	na	26	na	37	20–80	
SHAPS	na	14	na	14	na	14	14–56	
VVIQ	na	32	na	44	na	49	16–80	Higher score corresponds to less vivid imagery