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Dopamine and light: effects on facial emotion recognition

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Abstract

Bright light can affect mood states and social behaviours. Here, we tested potential interacting effects of light and dopamine on facial emotion recognition. Participants were 32 women with subsyndromal seasonal affective disorder tested in either a bright (3000 lux) or dim light (10 lux) environment. Each participant completed two test days, one following the ingestion of a phenylalanine/tyrosine-deficient mixture and one with a nutritionally balanced control mixture, both administered double blind in a randomised order. Approximately four hours post-ingestion participants completed a self-report measure of mood followed by a facial emotion recognition task. All testing took place between November and March when seasonal symptoms would be present. Following acute phenylalanine/tyrosine depletion (APTD), compared to the nutritionally balanced control mixture, participants in the dim light condition were more accurate at recognising sad faces, less likely to misclassify them, and faster at responding to them, effects that were independent of changes in mood. Effects of APTD on responses to sad faces in the bright light group were less consistent. There were no APTD effects on responses to other emotions, with one exception: a significant light $\times$ mixture interaction was seen for the reaction time to fear, but the pattern of effect was not predicted a priori or seen on other measures. Together, the results suggest that the processing of sad emotional stimuli might be greater when dopamine transmission is low. Bright light exposure, used for the treatment of both seasonal and non-seasonal mood disorders, might produce some of its benefits by preventing this effect.

Keywords

Seasonal affective disorder, acute phenylalanine/tyrosine depletion, bright light, phototherapy, negative bias

Introduction

Individuals with seasonal affective disorder (SAD) experience impairments in mood, sleep, energy, appetite, and social functioning (Kasper et al., 1989; Rosenthal et al., 1984b). Bright light exposure can reverse these symptoms, normalising mood and enhancing agreeableness (aan het Rot et al., 2008; Kasper et al., 1989; Rosenthal et al., 1984b). The alterations in mood and social functioning might be related in part to changes in emotional facial recognition. While results have been mixed – attributed largely to methodological variation – there is some evidence that individuals at risk for depression have an attentional bias towards depression-congruent stimuli (e.g. sad faces) and this cognitive bias has been suggested to reflect a vulnerability to developing depression (Joormann et al., 2007a). For example, currently depressed medication-free individuals can exhibit attentional biases to sad faces (Gotlib et al., 2004) and greater recognition of sad faces relative to other expressions (Dalili et al., 2015; Gollan et al., 2010). Preliminary evidence suggests that, in young adults with depressive symptoms, mood can be elevated by emotion perception training (Penton-Voak et al., 2012).

The neurobiology of emotion recognition is not well understood but monoamines are implicated. Acute administration of the noradrenergic antidepressant, reboxetine (Harmer et al., 2003, 2009), and the selective serotonin reuptake inhibitor, citalopram (Murphy et al., 2009), increase sensitivity to happy faces. While citalopram, when given acutely, may also increase fear recognition (Browning et al., 2007), repeated administration

of citalopram and reboxetine (Harmer et al., 2004) have the opposite effect, decreasing fear recognition.

Dopamine might also be involved. Neuroimaging studies have identified increased responses to negative emotional stimuli in dopamine-innervated brain regions in patients with mood disorders, compared to healthy controls (Keedwell et al., 2005; Surguladze et al., 2005). Moreover, in both healthy and depressed participants, transiently decreasing dopamine synthesis shifts positive biases to negative ones, leading to faster responses to sad versus happy words on an affective go/nogo task (McLean et al., 2004; Roiser et al., 2005). In comparison, administration of the

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dopamine D2 receptor antagonist, sulpiride, can decrease accuracy of angry face recognition in healthy young men (Lawrence et al., 2002), while patients with Parkinson's disease taken off dopamine medication improve in their ability to learn from negative feedback (Frank et al., 2004). More generally, dopamine plays a key role in processing motivationally salient information (Berridge and Robinson, 2003), influencing mood and motivational states (Leyton, 2010; Nestler and Carlezon, 2006).

Light might be a contributing factor. In laboratory animals, there is evidence that light affects dopamine cell firing (Dominguez-Lopez et al., 2014), tyrosine hydroxylase (Deatss et al., 2015; Dulcis et al., 2013), dopamine D2 receptor expression (Dulcis et al., 2013), and depression-related behaviours (Dulcis et al., 2013; Leach et al., 2013). In humans, those who have greater exposure to sunshine have higher dopamine D2 receptor availability than people exposed to less sunshine (Tsai et al., 2011).

Previously, we transiently lowered dopamine synthesis in women with subsyndromal SAD exposed to either bright or dim light (Cawley et al., 2013). This lowered dopamine state led to lowered mood, agreeableness, energy and the motivation to work for monetary reward. The effects on energy and motivation were independent of light, while the effects on mood and agreeableness were seen in the dim light condition only. This study also included a facial emotion recognition (FER) task, the results of which are presented here. We hypothesised that reduced dopamine transmission, induced by acute phenylalanine/tyrosine depletion (APTD), would decrease positive FER response styles and increase negative FER response styles, particularly in the dim light condition.

Methods and materials

Participant recruitment

The study was approved by the Institutional Review Board of McGill University's Faculty of Medicine, and all participants provided written informed consent. The a priori determined sample size of 15 participants in each light group (dim, bright) would allow the detection of a main treatment difference of approximately 0.8 SD with a power of 80% when alpha is 0.05. For comparison purposes, the study was carried out in women as in a previous study using the acute tryptophan depletion method (aan het Rot et al., 2008, 2010). The power to measure the treatment by group interaction was expected to be the same as the power to measure the treatment effect because both effects were studied within subjects. Testing days were at least 3 days apart and all took place during the follicular phase (between day 1 and 14) of the menstrual cycle as identified by self-report, decreasing the influence of fluctuating gonadal hormones.

Participants were recruited with local advertisements seeking women who felt less energetic in winter than in summer. Individuals who expressed interest were scheduled for a laboratory assessment that included the structured clinical interview for the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV), non-patient edition, the short Michigan alcoholism screening test (Selzer et al., 1975), the Beck depression inventory (Beck et al., 1961), a self-rated version of the Hamilton rating scale for depression, seasonal affective disorders (Williams, 1988) and the seasonal pattern assessment questionnaire (SPAQ)

(Rosenthal et al., 1984a). The SPAQ includes the global seasonality scale (GSS), which assesses the degree of seasonal change on six dimensions: sleep, appetite, mood, energy, weight and social activity. Inclusion criteria were being between the age of 18 and 40 years, because seasonality is more common in this age range (Kasper et al., 1989), and a GSS score of 6 or more out of 24, which indicates at least mild seasonal changes in mood and behaviour. All women replied 'yes' to the question 'If you experience changes with the seasons, do you feel that these are a problem for you?' Exclusion criteria were any past or present axis I disorders, as defined by the DSM-IV-TR, a BDI score of 15 or higher, use of hormonal contraceptives in the previous 3 months, abnormal sleep patterns, any current medical illness or the use of psychotropic medications. A physician conducted a physical exam to confirm medical fitness.

Testing took place over three consecutive winter seasons (2008–2010) starting a week after daylight savings time began (first Sunday in November) and ending once clocks moved forward in the spring (second Sunday in March). More information on participant selection and characteristics are provided in Cawley et al. (2013).

Eighteen women were initially assigned to the dim light condition. Of these, two withdrew after the first test day (one reported side effects, one reported having used illicit drugs). Twenty women were initially assigned to the bright light condition. Of these, four withdrew after the first test day (three reported side effects, one reported time constraints). Four of the six women had received the APTD mixture.

Study design

Participants were randomly assigned, in blocks of four, to one of two groups: a dim or bright light condition. In both conditions, participants received the APTD mixture and the nutritionally balanced (BAL) control mixture on different days using a double-blind crossover design. The order of treatment was randomised and counterbalanced. The amino acid (AA) mixture composition and administration procedures were the same as those described previously (Leyton et al., 2000).

On each test day, participants ingested the APTD or BAL mixture. Changes in plasma tyrosine and prolactin levels were observed as soon as 1–3 hours after ingestion of the AA mixture, but effects may be maximal at 4–7 hours (McTavish et al., 1999, 2001), a period at which significant decreases in striatal dopamine release have been observed in positron emission tomography (PET) studies (Leyton et al., 2004; Montgomery et al., 2003). Thus, all tasks were administered between 4 and 6 hours post-ingestion of the AA mixture. Plasma AA analyses have been reported elsewhere (Cawley et al., 2013).

Experimental procedure

Each participant was tested individually at the Douglas Mental Health University Institute in a windowless, temperature-controlled and soundproof isolation suite free from external time cues, enhancing uniformity among sessions. Light intensity settings were verified with a calibrated light metre (IL1400A; International Light). Light was administered by ceiling-mounted banks of cool-white fluorescent lamps (4100 K, F32T8/TL841;

Philips Lighting, and F032/841; Sylvania) covered with filters emitting less than 1% of radiant energy up to 400 nm (Uvalite Plus; Plaskolite Inc.).

Participants kept a regular nocturnal sleep schedule for at least one week before each test day. Maintenance of a regular sleep–wake cycle was verified by daily phone calls to our time-stamped voicemail at bedtime and wake time and completion of a sleep–wake log (Table 1). Each participant arrived at the laboratory on the evening before their test days, at least one hour before their normal sleep time. Upon arrival, participants handed in all personal devices that indicated the time (e.g. cell phone), and were placed in the isolation suite, asked to complete a set of questionnaires, and screened for recent illicit drug use (triage panel for drugs of abuse; Biosite Diagnostics) and pregnancy. Lights were turned off at their habitual bedtime, and participants slept in total darkness for their average duration of sleep (7–9 hours), calculated from the week before.

The day before each test day, participants were asked to consume a low-protein diet provided by the investigators, as described previously (Cawley et al., 2013). The same diet was provided before both experimental sessions to maintain the double blind and standardise food intake the day before.

Experimental sessions. Test sessions began at each participant's normal wake time with an initial light setting of ~10 lux; if the participant was assigned to the dim light condition they remained in this light setting. For participants in the bright light condition, light intensity was gradually increased in three increments over a 15-minute span (~10, ~180 and ~3000 lux) and then remained at 3000 lux for the remainder of the test day. Participants were given 30 minutes to get ready for the day, after which time they completed morning questionnaires, had their vital signs recorded and had a blood sample taken. They were then given one of the AA mixtures. The FER task was administered approximately 4 hours post-ingestion. At the end of the test day, approximately 6.5 hours post-ingestion, participants had their vital signs reassessed, ingested a meal high in protein and carbohydrates to normalise their tyrosine levels, and were released. These results are part of a larger study that included additional computer tasks and mood ratings, details of which can be found in Cawley et al. (2013).

Mood ratings. Self-reported mood states were assessed using the 72-item bipolar profile of mood states (POMS), a questionnaire sensitive to transient fluctuations in subclinical mood states (Lorr et al., 1982). POMS scores were normalised to t-scores. Other self-report tests have been reported elsewhere (Cawley et al., 2013).

Side effects: Dizziness, headache and nausea are commonly reported following AA mixture ingestion (Nagano-Saito et al., 2008; Venugopalan et al., 2011) or exposure to bright light (Cawley et al., 2013). These three items were assessed using visual analogue scales (VAS) 100 mm in length.

Facial emotion recognition task. The FER task was identical to that used by van der Rot and colleagues (2010). Images were taken from the pictures of facial affect series (Ekman and Friesen, 1976). All faces are grayscale images of three male and three female models. Each model portrayed a neutral expression and six emotional faces (angry, disgusted, fearful, happy,

sad and surprised). The intensity of each expression was digitally morphed between the fully expressed emotion (100%) towards the neutral face (0%) in progressive increments of 10% (Young et al., 1997). The task has been validated in imaging studies in which each image has been shown to be proportional to its perceived intensity, to the accuracy of recognition and to the activation of specific brain regions (Blair et al., 1999; Hess et al., 1997).

A total of 366 faces were presented in a randomised order on a laptop computer screen. A fixation symbol appeared in the centre of the screen for 500 ms before each face. The list of facial expressions then appeared on response buttons in randomised order at the bottom of the screen with 0 ms delay. The participants were instructed to click as quickly possible on the response button corresponding to their perception of the emotion, using a mouse. Before starting the task, each subject completed a practice session with 24 faces from two different models.

Variables of interest included: (a) reaction time in ms; (b) accuracy; (c) non-detection; (d) misclassification for each emotion (angry, disgusted, fearful, happy, sad, surprised or neutral) and intensity (0–100%); and (e) speed–accuracy trade-off. A log transformation was applied to the reaction time data because the distribution of reaction times deviated significantly from normality. Accuracy was defined by the number of times the perceived emotion correctly matched the expressed facial emotion. Non-detection was defined by the number of times the perceived emotion did not match the expressed facial emotion and was instead perceived as neutral. Misclassification was defined as the emotion being incorrectly classified and perceived as another emotion. Speed–accuracy trade-off was calculated as the square root of speed divided by accuracy.

Statistical analyses

To investigate whether bright light exposure and the APTD mixture interacted or modulated performance on the FER task, mixed linear models were used for analyses (Gueorguieva and Krystal, 2004) with PROC MIXED in SAS 9.1.3 for Windows. The primary outcome variable was accuracy. Non-detection and misclassification were secondary outcome variables. Preliminary analyses examined whether there was an overall difference in task performance among the six emotions. Consistent with van der Rot et al. (2010), based on the finding that performance varied across emotions ($P < 0.0001$ for all main effects of emotion), the effects of the between-subjects factor light (bright, dim), the within-subjects factor mixture (B, T-), and their interaction were then analysed separately for each emotion. Type III tests were deemed significant if P values were below 0.05. Significant interaction effects were analysed post-hoc using simple contrasts that were Tukey–Kramer corrected for multiple comparisons. Findings are reported using estimated least-squares means and standard errors of the mean (SEM). As the study included counterbalanced repeated measures, the effect of order was tested for. Random effects were included in the model by using a random intercept. Residual correlation was addressed using the estimation method of maximum likelihood; the denominator degrees of freedom were computed by dividing the residual degrees of freedom into between-subject and within-subject portions.

As APTD can affect mood (Cawley et al., 2013; Leyton et al., 2000) and mood can alter emotional response styles (Bouhuys

Table 1. Average sleep time, wake time, and sleep duration during the week prior to study entry for each participant.

Dim light condition				Bright light condition			
Subjects	Avg sleep time	Avg wake time	Avg sleep duration	Subjects	Avg sleep time	Avg wake time	Avg sleep duration
1	23:00	7:00	8	17	23:30	7:30	8
2	1:30	9:30	8	18	0:00	8:00	8
3	0:30	7:00	6.5	19	0:00	8:00	8
4	23:00	7:00	8	20	23:00	8:00	9
5	23:30	10:30	11	21	1:30	10:00	8.5
6	23:00	7:00	8	22	1:00	8:00	7
7	0:00	11:00	11	23	0:00	8:00	7
8	23:00	8:00	9	24	23:00	8:00	9
9	23:00	7:45	8.75	25	0:30	9:00	8.5
10	0:30	7:00	6.5	26	0:00	9:00	9
11	23:00	7:00	8	27	23:30	8:30	9
12	0:30	9:00	8.5	28	0:30	9:00	8.5
13	23:00	9:00	10	29	23:00	8:00	9
14	23:00	8:00	9	30	0:00	9:00	9
15	0:00	9:00	9	31	0:30	8:30	8
16	22:00	7:00	8	32	0:00	9:00	9
Average sleep duration			8.58	Average sleep duration			8.41

Avg: average.

et al., 1995), all analyses were run with the addition of participants' POMS total mood score included as a covariate, as in aan het Rot et al. (2010), using POMS scores collected immediately prior to subjects starting the FER task (4 hours post-AA mixture ingestion). Analyses of accuracy, non-detection and misclassification were completed for the six different facial expressions. In all of the reported data, the potential influence of side effects was controlled for by including a composite measure of dizzy, nauseous and headache visual analogue scores as a covariate. This composite variable was derived by taking the average of the three scales collected immediately before FER testing.

The estimated least-squares means and SEM were used to present all findings. The statistical analysis plan presented here is identical to that of aan het Rot and colleagues (2010).

Results

Participants

Thirty-two women completed the study. Of the 16 randomly assigned to the dim light group, nine received BAL on their first test day and seven received APTD. Of the 16 assigned to the bright light group, eight received BAL on their first day and eight received APTD. Participant GSS scores ranged from 7 to 16 out of 24 ($M=10.6$, $SD=2.5$). As none of the participants reported major depressive episodes, but all described clinically relevant symptoms during the winter months, participants were classified as having subsyndromal SAD. The average participant age was 23.0 ($SD 4.8$) years, and BDI scores averaged 3.13 ($SD 3.44$).

Overall performance per emotion

Performance varied among the six facial emotions ($F_{5,155}=67.94$, $P<0.0001$; see Table 2). Overall, participants were most accurate at rating happy faces and least accurate at recognising sad,

disgusted and fearful faces (Table 2). Non-detection ($F_{5,155}=22.39$, $P<0.0001$) and misclassification ($F_{5,155}=73.98$, $P<0.0001$) exhibited rankings similar to those seen for accuracy (Table 2). These rankings are similar to those seen previously (aan het Rot et al., 2010).

Accuracy

The mixed model yielded a significant light * AA mixture interaction for the recognition accuracy of sad faces ($F_{1,29}=5.25$, $P=0.02$) (Figure 1), and this remained significant when the side effects composite score was added as a covariate ($F_{1,29}=4.68$, $P=0.04$). Post-hoc comparisons revealed that participants in the dim light condition were more accurate at recognising sad faces following APTD (31.85 ± 1.58) compared to BAL (27.65 ± 1.56 ; $t_{29}=-2.74$, $P=0.047$). There were no significant interactions for the other emotions (Table 3).

Misclassification

A significant light * AA mixture interaction was identified for sad face misclassification scores ($F_{1,29}=4.49$, $P=0.043$), and the P value remained close to the usual threshold when adding the side effects composite score as a covariate to the model ($F_{1,29}=3.88$, $P=0.058$). The pattern of effects resembled what was seen for sad face recognition accuracy, and participants in the dim light condition had lower misclassification scores for sad faces following APTD (10.45 ± 1.46) compared to BAL (12.87 ± 1.13 , $P<0.05$). There were no significant interactions for the other emotions (Table 3).

Non-detection

There were no effects of APTD on non-detection, although there was a main effect of light for surprise ($F_{1,30}=4.93$, $P=0.034$)

Table 2. Accuracy, missclassification, and non-detection scores for the six emotions.

Accuracy			Misclassification			Non-detection		
High to lowest	Mean	SD	Low to highest	Mean	SD	Low to highest	Mean	SD
Happy ^{a,d,f,sa,su}	41.6	0.8	Happy ^{a,d,f,sa,su}	4.2	0.8	Disgusted ^{sa,su}	13.9	0.8
Surprised ^{d,f,h,sa}	33.7	0.8	Surprised ^{d,f,h}	10.1	0.8	Fearful ^{sa}	14.3	0.8
Angry ^{d,f,h,sa}	33.3	0.8	Sad ^{d,f,h}	11.1	0.8	Happy ^{sa}	14.9	0.8
Sad ^{a,h,su}	29.1	0.8	Angry ^{d,f,h}	11.6	0.8	Angry ^{sa}	15.2	0.8
Fearful ^{a,h,su}	27.3	0.8	Fearful ^{a,h,sa,su}	18.5	0.8	Surprised ^{d,sa}	16.1	0.8
Disgusted ^{a,h,su}	27.1	0.8	Disgusted ^{a,h,sa,su}	18.9	0.8	Sad ^{a,d,f,h,su}	19.8	0.8

The results are collapsed across treatment conditions. Mean scores are out of a maximum possible score of 60 per facial emotion. Superscript letters designate significant differences ($p < 0.05$) from (a) anger, (d) disgust, (f) fear, (h) happiness, (sa) sadness, and (su) surprise.

Figure 1. Sad facial emotion accuracy score and light condition.

reflecting higher rates of non-detection among participants tested in bright light (17.78 ± 1.03) compared to those tested in dim light (14.63 ± 0.97). When adding the side effects composite score as a covariate to the model, the result remained significant ($F_{1,30} = 4.67$, $P = 0.039$). There were no significant interaction effects (Table 3).

Response time

A significant light * AA mixture interaction was found for reaction times to sad faces ($F_{1,29} = 4.76$, $P = 0.039$), and this remained significant after adding the side effects score as a covariate ($F_{1,29} = 4.68$, $P = 0.04$). The post-hoc simple contrasts were non-significant (all P values > 0.14), but the pattern of effects for sad faces was similar to that seen for sad face recognition accuracy and misclassification. Participants in the dim condition had faster reaction times to sad faces following APTD (2.83 ± 0.026) compared to their reaction time following BAL (2.8 ± 0.026). A significant light * AA mixture interaction was also found for reaction times to fearful faces ($F_{1,2} = 4.40$, $P = 0.045$), although the post-hoc simple contrasts were non-significant (all P values > 0.09) and the pattern of effect was not predicted a priori or seen on other measures. There were no significant interactions for the other emotions (Table 3).

Speed–accuracy trade-off

In the present study both speed and accuracy for sad faces increased following APTD for those subjects tested in the dim

light group. To replicate the statistical plan from our previous paper (aan het Rot et al., 2010), analysis of speed–accuracy trade off was again assessed. A significant light * AA mixture interaction was found for sad faces ($F_{1,29} = 7.81$, $P = 0.009$), and this too remained significant after adding the side effects score as a covariate to the model ($F_{1,29} = 7.13$, $P = 0.012$). Inspection of this interaction indicated that there was a significant difference between the AA mixtures in the dim light group only ($P = 0.047$). Participants in the dim condition had higher speed–accuracy trade-off scores to sad faces following APTD (0.22 ± 0.01) compared to BAL (0.19 ± 0.01). Thus, individual differences in the improved sad face recognition accuracy were associated with increased time spent evaluating the faces. As APTD also tended to decrease sad face response times in the dim light condition, the speed–accuracy trade-off effect might reflect the greater focus on sad faces and more efficient use of time. There were no significant interactions for the other emotions (Table 3).

Influence of treatment order

The analyses for sadness were repeated with the between-groups factor order (APTD first, BAL first) included in the models. For accuracy, there was no significant mixture * order * light interaction ($P > 0.33$). The mixture * light interaction was no longer significant ($P = 0.361$), but there was a significant mixture * order interaction ($P < 0.001$), which revealed that only participants who received APTD second showed improved sadness recognition accuracy following APTD ($P = 0.006$). Analyses for each light

Table 3. Statistical analyses of the effects of light intensity and amino acid mixture for the six emotions.

	Anger	Disgust	Fear	Happy	Sad	Surprised
Accuracy						
Main effect of light	F(1,30)=0.12 P=0.73	F(1,30)=0.67 P=0.42	F(1,30)=0.52 P=0.47	F(1,30)=0.09 P=0.77	F(1,30)=0.45 P=0.51	F(1,30)=0.13 P=0.73
Main effect of APTD	F(1,29)=0.09 P=0.77	F(1,29)=0.30 P=0.59	F(1,29)= 0.80 P=0.38	F(1,29)=0.36 P=0.55	F(1,29)=2.68 P=0.11	F(1,29)=0.17 P=0.68
APTD * light interaction	F(1,29)=0.04 P=0.85	F(1,29)=0.33 P=0.57	F(1,29)=0.05 P=0.83	F(1,29)=2.45 P=0.13	F(1,29)=5.25 P=0.03	F(1,29)=0.73 P=0.40
Non-detection						
Main effect of light	F(1,30)=0.45 P=0.51	F(1,30)=0.29 P=0.59	F(1,30)=3.26 P=0.08	F(1,30)=0.02 P=0.89	F(1,30)=1.59 P=0.22	F(1,30)=4.93 P=0.03
Main effect of APTD	F(1,29)=0.51 P=0.48	F(1,29)=0.23 P=0.63	F(1,29) = 0.01 P=0.93	F(1,29)=1.49 P=0.23	F(1,29)=1.99 P=1.17	F(1,29)=0.17 P=0.68
APTD * light interaction	F(1,29)=1.10 P=0.30	F(1,29)=0.48 P=0.50	F(1,29)=0.84 P=0.37	F(1,29)=1.50 P=0.23	F(1,29)=0.66 P=0.43	F(1,29)=0.54 P=0.47
Misclassification						
Main effect of light	F(1,30)=0.09 P=0.76	F(1,30)=0.10 P=0.75	F(1,30)=0.00 P=0.97	F(1,30)=0.00 P=0.96	F(1,30)=0.76 P=0.39	F(1,30)=1.95 P=0.17
Main effect of APTD	F(1,29)=0.02 P=0.89	F(1,29)=0.65 P=0.43	F(1,29)=0.13 P=0.73	F(1,29)= 0.26 P=0.61	F(1,29)= 0.56 P=0.46	F(1,29)= 0.05 P=0.83
APTD * light interaction	F(1,29)= 0.23 P=0.63	F(1,29)= 0.01 P=0.92	F(1,29)= 0.44 P=0.51	F(1,29)= 0.70 P=0.41	F(1,29)= 4.49 P=0.04	F(1,29)= 0.06 P=0.81
Speed						
Main effect of light	F(1,30)=2.27 P=0.14	F(1,30)=3.49 P=0.07	F(1,30)=2.69 P=0.11	F(1,30)=1.69 P=0.20	F(1,30)=1.76 P=0.19	F(1,30)=2.86 P=0.10
Main effect of APTD	F(1,29)=0.04 P=0.85	F(1,29)=0.50 P=0.48	F(1,29)=1.43 P=0.24	F(1,29)=0.12 P=0.73	F(1,29)=0.51 P=0.48	F(1,29)=0.00 P=0.98
APTD * light interaction	F(1,29)=3.05 P=0.09	F(1,29)=1.27 P=0.27	F(1,29)=4.40 P=0.04	F(1,29)=1.16 P=0.29	F(1,29)=4.76 P=0.04	F(1,29)=1.21 P=0.28
Speed–accuracy trade-off						
Main effect of light	F(1,29)=2.34 P=0.34	F(1,30)=0.23 P=0.63	F(1,30)=0.29 P=0.59	F(1,30)=1.59 P=0.22	F(1,30)=0.37 P=0.55	F(1,30)=0.86 P=0.36
Main effect of APTD	F(1,29)=0.08 P=0.78	F(1,29)=0.01 P=0.94	F(1,29)=0.03 P=0.86	F(1,29)=0.00 P=0.94	F(1,29)=1.35 P=0.25	F(1,29)=0.01 P=0.94
APTD * light interaction	F(1,29)=2.34 P=0.14	F(1,29)=0.50 P=0.49	F(1,29)=2.22 P=0.15	F(1,29)=2.52 P=0.12	F(1,29)=7.81 P=0.01	F(1,29)=2.10 P=0.15

APTD: acute phenylalanine/tyrosine depletion.

condition separately confirmed that this improvement occurred in dim ($P=0.006$) but not in bright light ($P=0.48$).

For misclassification, there was no significant mixture * order * light interaction ($P>0.75$). The mixture * light interaction was no longer significant ($P=0.343$). There was a significant mixture * order interaction ($P=0.002$). All post-hoc contrasts were non-significant, but analyses for each light condition separately found that, in participants who received APTD first, an APTD-induced increase in sadness misclassification occurred in bright ($P=0.04$) but not dim light ($P=0.71$).

For speed, there was no significant mixture * order * light interaction ($P>0.16$). The mixture * light interaction was no longer significant ($P=0.317$). There was a significant mixture * order interaction ($P=0.0002$), which revealed that only participants who received APTD second became faster at sadness recognition following APTD ($P=0.004$). Analyses for each light condition separately showed that this improvement tended to occur in both dim ($P=0.07$) and bright light conditions ($P=0.03$).

For speed–accuracy trade-off, there was no significant mixture * order * light interaction ($P>0.75$). The mixture * light interaction was no longer significant ($P=0.13$). There was a significant mixture * order interaction ($P<0.0001$), which revealed that APTD reduced speed–accuracy trade-off scores in participants who received APTD first ($P=0.027$) and increased scores in participants who received APTD second ($P=0.0004$). Analyses for each light condition separately revealed that the former occurred in bright ($P=0.0015$) but not in dim light ($P=0.81$) and the latter occurred in both dim ($P=0.0027$) and bright light ($P=0.0490$). For non-detection there were no significant interaction effects involving order ($P>0.21$).

Discussion

This study investigated whether transiently decreasing dopamine transmission would alter the recognition of emotional faces in people with subsyndromal SAD. As predicted, APTD improved

sad face recognition in participants who spent a day in dim light (~10 lux), an effect seen less consistently in bright light (~3000 lux). APTD did not significantly increase the recognition of other negative emotional faces (i.e. disgust, anger, fear) or decrease the recognition of happy faces. The reasons for this are unclear but might reflect features of the test population (women with subsyndromal SAD), their susceptibility to sad emotional states, and consequently the greatest ability of this particular test stimulus to uncover an effect.

A transient decrease in dopamine transmission could be adaptive in healthy people, enhancing their ability to learn about and avoid negative events (Cox et al., 2015; Frank et al., 2004). In comparison, in vulnerable individuals an enhancement of sad face recognition might contribute to depressive states perhaps particularly if the effect was sustained and combined with other influences of low dopamine states on motivational drive (Barrett et al., 2008; Cawley et al., 2013; Venugopalan et al., 2011). Likely aggravating these effects, decreases in dopamine transmission in people with mood disorders (Nestler and Carlezon, 2006) most probably occur in combination with disturbances to other neural systems (Hamon and Blier, 2013).

Recent studies provide accumulating evidence that attentional biases influence susceptibility to clinically relevant states. Both current and remitted depressed patients, as well as adolescent girls at high risk of depression, exhibit attentional biases specifically for sad faces (Joormann and Gotlib, 2007; Joormann et al., 2007a, 2007b), and attentional bias training using happy and sad facial stimuli has been shown to diminish stress-related psychophysiological responses in girls at elevated risk for depression (LeMoult et al., 2016). The clinical efficacy of bright light therapy for both seasonal (Kasper et al., 1989; Rosenthal et al., 1984a) and non-seasonal mood disorders (Rosenthal et al., 1984b; Sahlem et al., 2014) might be related in part to an ability to reverse low dopamine-related effects on these processes.

Limitations

The results presented here should be considered in light of the following. First, 32 volunteers were tested. This is quite respectable compared to other AA depletion studies, particularly considering the carefully controlled testing conditions, such as having participants arrive the night before, sleep in identical environments, and then experience calibrated changes in light exposure. This noted, 32 subjects is ultimately a small sample size, and it remains possible that not all of the effects of the APTD and light exposure manipulations were captured. As all participants were women, it also remains unknown whether the effects generalise to men. Second, the studied sample was relatively healthy and the results might not be generalisable to populations with more severe symptoms. For example, two studies (Mah and Pollock, 2010; Schaefer et al., 2010) did not find evidence of increased sad facial recognition in medication-free depressed patients. However, those studies included features that differed from the study that identified differences (Gollan et al., 2010). In Mah and Pollock (2010), the participants had late life depression onsets, and there is evidence that this subgroup has neurobiological features that differ from those with an early to mid-life onset (Van den Berg et al., 2001). In Schaefer et al. (2010), the researchers used a different FER task, relying on animated rather than finely

grained static images, raising the possibility that the latter method can detect subtler changes (Gollan et al., 2010). Third, there were some unexpected effects of order, with APTD sometimes influencing FER when it was given on test day 1, other times when it was given on day 2. The reasons for these effects are unclear, but overall they do not change the central finding that APTD enhanced the recognition of sad faces. Fourth, as with any study using light levels as a manipulation it is difficult to 'blind' the condition of light. However, the influence of light was only seen in combination with the AA mixtures which were administered in a double-blind fashion. No independent effects of light were observed, which suggests that knowledge of the light manipulation did not significantly influence the results. Fifth, the effects of APTD on sad face recognition variables were consistent across the various outcome measures, but the effects were not large and additional effects on the recognition of other emotions may have been missed. Replication, as for any new observation, will be critical. Finally, dopamine can be converted to norepinephrine by dopamine- β -hydroxylase, and APTD might also affect norepinephrine. However, studies in laboratory rats suggest that APTD decreases norepinephrine synthesis less than dopamine synthesis (McTavish et al., 1999) and decreases the neuronal release of dopamine but not norepinephrine (Le Masurier et al., 2013; McTavish et al., 1999; Shnitko et al., 2016). In humans, APTD decreases dopamine release, as measured by PET (Leyton et al., 2004; Montgomery et al., 2003), and increases the release of prolactin, a neuroendocrine index of lowered dopamine transmission (Harmer et al., 2001; McTavish et al., 2001), without altering circulating levels of melatonin, a neuroendocrine index of norepinephrine transmission (Sheehan et al., 1996).

Conclusion

We have presented data suggesting that, in mildly seasonal women, APTD increases the recognition of sad facial expressions, particularly when administered in dim light. A combination of low dopamine with dim light might influence susceptibility to symptoms of winter depression.

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