Flinders
UNIVERSITY

Genetic correlations between wellbeing, depression and anxiety symptoms and behavioral responses to the emotional faces task in healthy twins

Kylie M. Routledge , Leanne M. Williams , Anthony W.F. Harris , Peter R. Schofield , C. Richard Clark , Justine M. Gatt

PII: S0165-1781(17)32081-4
DOI: 10.1016/j.psychres.2018.03.042
Reference: PSY 11274

To appear in: *Psychiatry Research*

Received date: 13 November 2017
Revised date: 5 March 2018
Accepted date: 18 March 2018

Please cite this article as: Kylie M. Routledge , Leanne M. Williams , Anthony W.F. Harris , Peter R. Schofield , C. Richard Clark , Justine M. Gatt , Genetic correlations between wellbeing, depression and anxiety symptoms and behavioral responses to the emotional faces task in healthy twins, *Psychiatry Research* (2018), doi: 10.1016/j.psychres.2018.03.042

Highlight

- Twin study examining wellbeing, depressive symptoms and emotion processing
- Significant phenotypic associations between depression, wellbeing and happy faces
- Association between depression and anxiety symptoms and happy faces driven by genetics
- Phenotypic association between depression and anxiety symptoms and neutral faces

Genetic correlations between wellbeing, depression and anxiety symptoms and behavioral responses to the emotional faces task in healthy twins

Kylie M. Routledge[a], Leanne M. Williams[b], Anthony W.F. Harris[a,c], Peter R. Schofield[d,e], C. Richard Clark[f], Justine M. Gatt[d,g]

[a]The Brain Dynamics Centre, Westmead Institute for Medical Research, University of Sydney, Westmead, NSW 2145, Australia

[b] Department of Psychiatry and Behavioral Sciences, Stanford School of Medicine, Stanford University, Stanford, California 94305-5717, United States of America

[c] Discipline of Psychiatry, Sydney Medical School, University of Sydney, NSW 2006, Australia

[d] Neuroscience Research Australia, Randwick NSW 2031, Australia

[e] School of Medical Sciences, University of New South Wales, Sydney, NSW 2052, Australia.

[f] School of Psychology, Flinders University, Bedford Park, South Australia, 5042, Australia

[g] School of Psychology, University of New South Wales, Sydney NSW 2052, Australia.

***Corresponding author:**

Dr Justine M Gatt; Phone (+61 2 9399 1812); E-mail address: j.gatt@neura.edu.au

Postal address: Neuroscience Research Australia, Barker St, Randwick Sydney NSW 2031 Australia.

Running head: Wellbeing and emotion processing in twins

Word count:
Abstract (word count): 185
Text (word count): 5,122
Tables: 4
Figures: 1
Supplementary Materials: 2

Authors contact details (phone/email/postal address):

Kylie M. Routledge; (+61 2) 8627 3305; kdow5762@uni.sydney.edu.au; The Brain Dynamics Centre, Westmead Institute for Medical Research, University of Sydney Westmead, NSW 2145, Australia.

Leanne M. Williams; (+1 650) 723 3579; leawilliams@stanford.edu; Department of Psychiatry and Behavioral Sciences, Stanford School of Medicine, Stanford University, Stanford, California 94305-5717, United States of America.

Anthony W. Harris; (+61 2) 9845 6688; anthony.harris@sydney.edu.au; Discipline of Psychiatry, Sydney Medical School & Westmead Institute for Medical Research, University of Sydney Westmead, Westmead, NSW 2145, Australia.

Peter R Schofield; (+61 2) 9399 1603; p.schofield@neura.edu.au; Neuroscience Research Australia, Barker St, Randwick Sydney NSW 2031 Australia.

C. Richard Clark; (+61 8) 8410 6500; richard.clark@brainhealth.com.au; School of Psychology, Flinders University, Bedford Park, South Australia, 5042, Australia.

Dr Justine M Gatt; (+61 2) 9399 1812; j.gatt@neura.edu.au; Neuroscience Research Australia, Barker St, Randwick Sydney NSW 2031 Australia.

Disclosure Statement

KMR, PRS and CRC have no conflicts of interest to report. AWFH has consulted for Lundbeck Australia and received fees for lectures from Janssen-Cilag and Lundbeck Australia. He has been an investigator on industry sponsored trials by Janssen-Cilag and Brain Resource Ltd. CRC holds a small quantum of stock in Brain Resource Ltd and has received fees from Brain Resource Ltd for consultancies unrelated to this study. LMW has received fees for consultancies unrelated to this study and previously held stock options from Brain Resource Ltd. JMG is a stockholder in MAP Corp. Pte Ltd.

Abstract

Currently there is a very limited understanding of how mental wellbeing versus anxiety and depression symptoms are associated with emotion processing behaviour. For the first time, we examined these associations using a behavioural emotion task of positive and negative facial expressions in 1668 healthy adult twins. Linear mixed model results suggested faster reaction times to happy facial expressions was associated with higher wellbeing scores, and slower reaction times with higher depression and anxiety scores. Multivariate twin modelling identified a significant genetic correlation between depression and anxiety symptoms and reaction time to happy facial expressions, in the absence of any significant correlations with wellbeing. We also found a significant negative phenotypic relationship between depression and anxiety symptoms and accuracy for identifying neutral emotions, although the genetic or environment correlations were not significant in the multivariate model. Overall, the phenotypic relationships between speed of identifying happy facial expressions and wellbeing on the one hand, versus depression and anxiety symptoms on the other, were in opposing directions. Twin modelling revealed a small common genetic correlation between response to happy faces and depression and anxiety symptoms alone, suggesting that wellbeing and depression and anxiety symptoms show largely independent relationships with emotion processing at the behavioral level.

Key words: well-being, COMPAS-W, resilience, DASS, emotion processing

1. Introduction

Seventy years ago, the World Health Organisation (WHO) enshrined into its Constitution a definition of health that included a "complete state of physical, mental and social wellbeing and not merely the absence of disease or infirmity …(but) the highest attainable standard of health" (WHO, 1946, p. 1). Research into mental wellbeing is now starting to thrive, yet we still do not know much about the underlying neuropsychological mechanisms that characterise different levels of wellbeing. One thing is clear: the absence of mental illness does not necessarily indicate the presence of optimal mental wellbeing. Previous research has shown that mental wellbeing and mental illness constitute two separate correlated axes, sharing only about 25% in common variance (Keyes, 2005). This accords broadly with our own findings in 1486 healthy adult twins for which we found that only 34% of total variance in wellbeing scores was shared with symptoms of depression and anxiety (Routledge et al., 2016). Together, this suggests that mental wellbeing and illness symptoms are largely two separate constructs, so when trying to explore underlying neuropsychological mechanisms of mental health, it is important to consider both constructs as key primary outcomes.

One form of neuropsychological processing that is essential to mental health is emotion processing. Emotion is fundamental to our identity, and wide-ranging in its influence on memory and decision-making (Damasio, 1994). It promotes interpersonal connection, communicates intentions (Sroufe, 1995) and forms a primary source of motivation to act in ways that minimize danger and maximize reward (Williams, Gatt, et al., 2008). Emotion processing is a key aspect of emotional function which broadly encompasses identifying, processing and interpreting emotions, as well as making inferences about the emotional state and intentions of others (Weightman, Air, & Baune, 2014). Neural networks associated with emotion processing include prefrontal regions – important in emotion regulation, cognitive

control and executive function; the amygdala – involved in processing emotional stimuli; and the ventral striatum – implicated in motivated behaviour and reward (MacQueen, 2012). Impairments in emotion processing are a hallmark of mood disorders and a substantial literature has linked facial emotion processing dysfunction with disorders such as schizophrenia, depression and Attention Deficit Hyperactivity Disorder (ADHD) (Barkl, Lah, Harris, & Williams, 2014; Elliott, Zahn, Deakin, & Anderson, 2011; Gur & Gur, 2016; MacQueen, 2012; Weightman et al., 2014; Williams, Hermens, et al., 2008). In a review by Weightman et al. (2014), patients with Major Depressive Disorder (MDD) were reported to have negative biases in identifying emotional expressions (i.e., identifying neutral faces as sad or angry) and impairments in recognizing happy expressions. Similar attentional biases towards threat have been reported in clinical and non-clinical anxious populations (Bar-Haim, Lamy, Pergamin, Bakermans-Kranenburg, & Van Ijzendoorn, 2007), suggesting a core attentional bias towards negative emotions across levels of severity.

In healthy populations, the observation of patterns of emotional processing biases with wellbeing is much sparser. One small study in 28 healthy young adults (mean age of 21.6 years) found that participants with high and low subjective wellbeing both identified positive words more quickly and accurately than negative words, but participants with greater subjective wellbeing showed a reduced priming response to negative stimuli (Yu & Li, 2012), suggesting that participants with greater subjective wellbeing were less sensitive to fear stimuli. Positive attentional biases have also been reported. In a sample of 30 healthy adults (aged 18-50 years), higher life satisfaction was linked with faster reaction times for identifying happy faces (Vittersø, Oelmann, & Wang, 2009). Another study similarly reported that positive attentional biases were related with increased positive mood in a sample of 83 young adults (mean age of 22.2 years) (Sanchez & Vazquez, 2014). To our knowledge, these are the only studies that have examined associations between facial

emotion processing and wellbeing in healthy adults. Although they have shown a relationship between attentional biases in face processing and mood, not all studies included both measures of mental wellbeing and mental illness (i.e., negative mood symptoms). Moreover, for those studies that included both measures, none to date have examined the covariance between wellbeing and negative mood symptoms to evaluate the common versus specific relationships that may exist with emotion processing. The sample sizes of these studies were also quite small and often with a limited focus on young adults. Hence, there is a need to examine associations between emotion processing and both wellbeing and negative mood symptoms in one large age-heterogeneous healthy sample.

One powerful way of understanding the association between emotion processing and its common versus specific links with wellbeing and illness symptoms is by using the twin design. The comparison of identical (monozygotic; MZ) to non-identical (dizygotic; DZ) twins is a powerful method of defining the genetic and environmental influences on a variable, and between variables. As MZ and DZ twins are thought to share a common environment but differ in terms of genetics (MZ twins having 100% common genetics versus DZ twins with 50% common genetics), if MZ twins show significantly increased similarity on a measure than DZ twins, it is thought to be a result of genetic factors, and the size of this effect is measurable using twin modelling. Previous twin studies show the heritability of wellbeing and depression and anxiety symptoms is small to moderate (30-48%; Bartels, 2015; Burton et al., 2015; Gatt, Burton, Schofield, Bryant, & Williams, 2014). Fewer twin studies have examined the heritability of emotion processing, and of those that have, the studies typically employ facial recognition tasks that involve the identification (i.e., correct labelling) or recognition of previously-presented emotions. Heritability estimates reported are mostly small and similar across age, ranging from 36% for emotion identification in healthy children and young adults aged 8 to 21 years (Robinson et al., 2015) to 32% in adults

(Knowles et al., 2015). We are not aware of any twin studies that have yet examined the covariance between emotional function, wellbeing and symptoms of depression and anxiety to test whether wellbeing and mental illness symptoms have independent or common associations with emotional function.

Evidence to date has so far shown a common genetic link between aspects of emotional function and depression and anxiety symptoms. Genetic variation has been shown to differentially impact the neural and behavioral processing of happy and sad faces (Chakrabarti, Kent, Suckling, Bullmore, & Baron-Cohen, 2006; Domschke et al., 2008; Matsunaga et al., 2014) in regions critical in reward processing, and which are associated with depression and anxiety symptoms (Dillon et al., 2014). In contrast, genetic influences for any common associations between emotion processing and wellbeing are unknown. However, given that roughly a quarter to a third of variance in wellbeing is shared with depression and anxiety (Keyes, 2005; Routledge et al., 2016), it is reasonable to suppose that some common genetic influences may exert opposing effects on wellbeing and symptoms of mental illness.

In the current study, we sought to examine the relationship between emotional function, mental wellbeing and depression and anxiety symptoms in healthy adult twins spanning 18 to 62 years of age. We hypothesised that there would be both independent and common associations of wellbeing and depression and anxiety symptoms with emotion processing. After identifying associative relationships using linear mixed models, we sought to explore the genetic and environmental influences on emotion processing, and their covariation with wellbeing and depression and anxiety symptoms. We hypothesised that there would be both common and independent genetic influences contributing to total variance in emotion processing. To achieve this, we used twin modelling to derive the heritability of two forms of

emotion processing: explicit emotion identification and implicit emotion bias for each emotion (happy, sad, anger, fear, disgust and neutral). We then modelled these genetic and environmental correlations of emotion processing with wellbeing and depression and anxiety symptoms. Twin pair data was extracted from the Twin study of Wellbeing using Integrative Neuroscience of Emotion (TWIN-E) (Gatt et al., 2012). Mental wellbeing and depression and anxiety symptoms were measured using the COMPAS-Wellbeing scale (the COMPAS-W; Gatt et al., 2014) and the Depression-Anxiety-Stress Scale (DASS-42) (Lovibond & Lovibond, 1995), respectively. Explicit emotion identification and implicit emotion bias were assessed using a previously validated computerized assessment, WebNeuro (Mathersul et al., 2009; Silverstein et al., 2007).

2. Methods and Materials

2.1 Participants

Participants were drawn from the TWIN-E Study conducted at the Brain Dynamics Centre and the University of Sydney (Gatt et al., 2012). Participants were healthy, same-sex twin pairs recruited by the Australian Twin Registry, with European ancestry (to avoid population stratification effects in genetic analysis) and English as their primary language. Exclusion criteria included current or lifetime psychiatric illness, history of stroke or neurological disorder, genetic disorder, brain injury (causing loss of consciousness for more than 10 minutes), chronic and serious medical conditions (e.g., cancer, heart disease), blood-borne illnesses, substance abuse, or visual impairments not corrected by glasses/lenses. The study was approved by the Human Research Ethics Committees of the University of Sydney (03-2009/11430) and Flinders University (FCREC#08/09), and participants provided written consent prior to participation.

This study included 1668 monozygotic (MZ) and dizygotic (DZ) twins ranging in age from 18 to 62 years. Demographic characteristics are contained in Table 1. The age range was selected to include the age-of-onset for most common psychiatric disorders. Children under 18 and adults over 65 were excluded to minimise the effects of neurodevelopmental changes in adolescence and neurodegeneration in old age. Zygosity was confirmed by DNA testing.

[INSERT TABLE 1 ABOUT HERE]

2.2 Measures

The protocol for this study has been published previously (Gatt et al., 2014; Gatt et al., 2012). In this baseline phase of the study, participants completed WebQ, a battery of online self-report questionnaires, and WebNeuro, a series of cognitive tasks measuring emotional function.

2.2.1 Mental wellbeing

We used the 26-item COMPAS-W scale (Gatt et al., 2014) which provides a measure of composite wellbeing (i.e., both hedonic and eudaimonic aspects of wellbeing) as well as subscale scores for Composure (competency and adaptability in stressful situations), Own-worth (autonomy and independent self-worth), Mastery (self-confidence and perceived control over one's environment), Positivity (optimism and positive outlook), Achievement (goal orientation and striving) and Satisfaction (satisfaction with life, health, work, personal relationships and emotions). The scale has strong internal reliability (total Wellbeing r=0.84, average r=0.71) and test-retest reliability over 12 months (total Wellbeing r=0.82, average r=0.62; Gatt et al., 2014).

2.2.2 Depression and anxiety risk symptoms

We used total scores from the Depression, Anxiety and Stress Scale (DASS-42; Lovibond & Lovibond, 1995) as a measure of depression and anxiety risk symptoms. The DASS-42 has been validated against the Beck Depression and Anxiety Inventory (Lovibond & Lovibond, 1995) and has been normed in both clinical and nonclinical populations. The DASS-42 subscales capture symptoms of depression (the Depression subscale), somatic symptoms of anxiety (Anxiety subscale), and chronic non-specific arousal (Stress subscale). Internal reliability for the Depression, Anxiety and Stress scales has been reported to be 0.91, 0.84 and 0.90, respectively (Lovibond, 1998). Test-retest reliability over 3 months for the Depression, Anxiety and Stress scales has been reported to be 0.59, 0.65 and 0.77, respectively (Gomez, Summers, Summers, Wolf, & Summers, 2014).

2.2.3 Emotional function

We used a computerized assessment, WebNeuro, to measure different components of emotional function: emotion identification and implicit bias (Mathersul et al., 2009; Silverstein et al., 2007; Williams et al., 2009). Reliability and validity has been previously established (Paul et al., 2005; Silverstein et al., 2007), and content validity confirmed using factor analysis (Mathersul et al., 2009). Construct validity has been established across touchscreen and paper-and-pencil versions (Paul et al., 2005). Test-retest reliability has been confirmed over 8 weeks (Williams et al., 2005) with estimates of 0.79 for measures of emotion identification and 0.72 for emotion bias (Brain Resource Ltd, 2010; Williams et al., 2009). Age, sex and education norms have been established for an Australian population in a sample of 1,000 healthy participants ranging in age from 6 to 92 years, and shown to be comparable to those established for a US sample (Mathersul et al., 2009; Williams et al., 2009). The emotion tasks include pictures of 72 facial expressions of five different emotions: happiness, fear, anger, sadness and disgust, as well as a neutral expression. The expressions

are derived from a standardized normed set (Gur et al., 2002) and include 12 individuals, of which half are male. Tasks for each domain have been previously described (Gatt et al., 2012) and are as follows:

(i) Explicit emotion identification: In the explicit phase of the task, pictures of eight (four male, four female) individuals displaying the six emotional expressions were presented for 2 seconds each in a pseudorandom sequence. Participants were instructed to select the label corresponding to the displayed emotion from a list of the six options. The measure for this task was accuracy and reaction time for accurately identified responses for each emotion.

(ii) Implicit emotion bias: A 20-minute interval of unrelated tasks followed the emotion identification task. Following this interval, 48 faces – four males and four females, displaying each of the six emotions – were presented in pseudorandom order. Half of the faces (i.e., two males and two females) had been presented in the previous explicit condition, and participants were instructed to click the faces they recognized from the original list. The measure was reaction time for accurately identified faces for each emotion minus the reaction time for accurately identified neutral faces. This measures implicit priming effects of each emotion.

Correlations between the emotion measures are presented in Supplementary Table 1.

2.3 Analyses

2.3.1 Association between emotional function, wellbeing and depression and anxiety symptoms

We tested all variables for normality. Extreme outliers (3+ SD from the mean) were replaced with the next most extreme score, and variables were transformed where appropriate using z-

score or log transformations to correct for any non-normality or skewness in the data, as indicated in the tables.

Pearson's correlation coefficients were used to check for relationships between age, education and all emotion, wellbeing, depression and anxiety symptom scores. Age and education were significantly correlated with several of the variables (see Supplementary Table 1, and so we covaried for age and education in all analyses. We then checked for sex differences for all emotion variables (see Supplementary Table 2). As there were several significant sex effects, sex was also included as a covariate in all analyses. To test for relationships between the emotion, wellbeing and DASS scores, we ran linear mixed models in SPSS Version 24. COMPAS-W and DASS-42 scores were entered (in separate models) as independent variables predicting emotion scores, with age, sex, education and zygosity included as fixed covariates. We incorporated family group as a random factor in order to allow for correlation within related twin pairs. We used the corrected *p*-value threshold of $p < .01$ to adjust for multiple comparisons.

2.3.2 Twin genetic modelling

Genetic modelling for complete twin pairs (n=1502; 751 complete pairs) was conducted in R studio version 3.0.3, using OpenMx version 1.4 (Boker, 2011; R Core Team, 2013). We removed three twin pairs with indeterminate zygosity. One variable, emotion identification accuracy for happy faces, was removed from the twin models as inspection revealed that most participants (92%) scored 100%. We also tested for multivariate normality and removed 8 twin pair outliers. The final sample for the twin modelling was therefore 1480 individuals, or 740 complete twin pairs. Demographic information for the sample is included in Table 1. Age, sex and education were included as covariates in all analyses.

a. Univariate modelling

Initially we decomposed the genetic and environmental influences of each of the emotion scores. We first inspected intra-class correlations to determine whether to fit an ACE (additive genetic, common environment and unique environment) or ADE (additive genetic, dominant genetic and unique environment) model. ADE models were considered appropriate when the DZ correlations were less than half the MZ correlation; ACE models where the DZ correlation was more than half the MZ correlation. After running the full ACE/ADE model, we tested nested sub-models by sequentially dropping A and C/D paths, using the *p* value associated with the difference in log likelihoods to indicate a significant change in model fit. As E contains measurement error, it is not appropriate to drop E paths. To compare model fit, we used the Akaike's information criterion (AIC) value, such that lower values indicated a better-fitting model (Keyes, Myers, & Kendler, 2010). Univariate models for wellbeing and depression and anxiety symptoms have already been established for this sample in previous studies (Burton et al., 2015; Gatt et al., 2014). We used the model-fitting results to guide the multivariate modelling. That is, previous univariate modelling had identified AE models as best-fitting for total depression and anxiety scores (Burton et al., 2015) and wellbeing (Gatt et al., 2014), so if univariate models suggested AE as best-fitting for a significant emotion variable, we used AE models in the multivariate testing.

b. Multivariate modelling

Where there were significant associations between wellbeing and/or depression and anxiety symptoms with the emotion processing variables in the linear mixed models, we used multivariate genetic modelling to examine the shared and unique nature of the relationships. A correlated-factors model was used to examine the genetic and environmental correlations between the variables, and nested models sequentially dropped each correlation to determine its significance. As in the univariate modelling, *p* values

associated with the log likelihood difference and lower AIC values were used to evaluate model fit. To identify the contribution of additive genetics to the phenotypic correlation between each pair of variables, we multiplied the absolute values for the genetic correlation by the square root of each heritability estimate (for example, $\sqrt{h^2}$ for the emotion score x $\sqrt{h^2}$ for wellbeing, multiplied by the genetic correlation). The environmental contribution was calculated similarly, but using the environmental correlation and estimates rather than the genetic contributions. Absolute values for the resulting figures, representing the genetic and environmental contributions to the relationship, were summed to give the phenotypic correlation. The proportion attributable to each was then calculated by dividing the relevant contribution by the phenotypic correlation.

3. Results

3.1 Descriptive correlations

Correlational analyses indicated that age, education and sex were significantly associated with emotion processing, depression and anxiety symptoms and wellbeing (Supplementary Table 1). Older age was associated with higher wellbeing, reduced depression and anxiety symptoms, slower reaction times for emotion processing of all explicit emotions, and faster (i.e., increased implicit attentional biases) for threat faces anger, disgust and fear. Higher levels of education were also associated with higher wellbeing, but faster explicit emotion processing reaction times for anger and disgust, and slower (i.e., reduced implicit attentional biases) for threat faces anger, disgust and fear. Sex comparisons (Supplementary Table 2) indicated that females showed significantly faster reaction times for emotion processing of all explicit emotions, and increased accuracy for the explicit identification of fearful faces. There were no sex differences for implicit emotion biases.

3.2 Linear mixed-effects models

The mixed model results are displayed in Table 2. For wellbeing, the only effect identified trending near significance (p = .02) was a negative association with explicit happy reaction time, whereby increased wellbeing was associated with faster reaction time to happy emotional expressions. The same emotion processing variable also showed a significant positive association with depression and anxiety symptoms, whereby higher depression and anxiety symptoms was associated with slower reaction time to happy emotional expressions. There was also a significant negative relationship between depression and anxiety symptoms and accuracy for explicit identification of neutral expressions, such that higher depression and anxiety scores related to decreased accuracy. No other emotional function variables showed any association with wellbeing or depression and anxiety symptoms.

[INSERT TABLE 2 ABOUT HERE]

3.3 Twin genetic modelling

3.3.1 Univariate modelling

Table 3 contains the intra-class correlations and heritability estimates for all models. Univariate modelling indicated that, in most cases, AE models were best-fitting; the three exceptions were accuracy for explicit identification of fear expressions, where an ACE model was most appropriate; and implicit bias for angry and sad expressions, where E models proved optimal. Fit statistics and parameter estimates are in Supplementary Table 3. Average additive genetic heritability ("A") for the different measures was as follows: Emotion Identification RT: 0.34 (ranging from 0.27 for happy RT up to 0.37 for fear/sad RT); Emotion identification accuracy: 0.24 (ranging from 0.23 for disgust/fear/neutral accuracy to 0.28 for

angry accuracy); and implicit Emotion Bias: 0.10 (ranging from 0.00 for implicit sad-neutral RT to 0.16 for implicit fear-neutral RT).

[INSERT TABLE 3 ABOUT HERE]

3.3.2 Multivariate modelling

Explicit emotion identification: Happy reaction time. The only significant relationship with wellbeing in the mixed models was explicit RT for identification of happy faces (albeit at trend-level significance of p=0.02), which also had a significant association with depression and anxiety symptoms (p=0.01; Table 2). We fit a multivariate model for the three variables in order to determine whether the relationship with wellbeing was independent of, or in common with, depression and anxiety symptoms. Fit statistics are contained in Table 4. The phenotypic correlation between wellbeing and explicit happy reaction time was 0.06 and was largely (82%) accounted for by additive genetic influences. Depression and anxiety symptoms showed similar results, with additive genetics forming the majority (79%) of the phenotypic correlation (r=0.11). In the correlated-factors model, only the genetic correlation (r=0.30) between explicit happy reaction time and depression and anxiety symptoms was significant. Both environmental correlations between wellbeing or depression and anxiety symptoms with happy reaction time were not significant.

Explicit emotion identification: Neutral accuracy. There was a significant relationship between depression and anxiety symptoms and accuracy for identification of Neutral expressions. We fit a bivariate model to examine the shared relationship between the two variables. Fit statistics are contained in Table 4. The phenotypic correlation between depression and anxiety symptoms and explicit neutral accuracy was 0.05, and was largely (67%) accounted for by nonshared environmental influences. However, neither environmental nor genetic correlations were significant in the twin model.

[INSERT TABLE 4 AND FIGURE 1 ABOUT HERE]

4. Discussion

In this study, we first aimed to assess the associative relationships between wellbeing, depression and anxiety symptoms and emotional processing in healthy adults. Linear mixed-effects models suggested that faster reaction times for accurately identifying happy faces was significantly associated with lower depression and anxiety scores, and with higher wellbeing (at trend level), whereas lower accuracy for identifying neutral expressions related to higher levels of depression and anxiety symptoms. No other significant associations between explicit emotion identification and implicit emotion bias were identified.

Firstly, a significant association was found between reaction times for happy faces and both depression and anxiety symptoms and wellbeing. Of the very few studies that have observed patterns of association between wellbeing and emotion processing, previous results generally suggest a response bias for quicker processing of happy faces than other emotions in individuals with higher wellbeing (Yu & Li, 2012); a pattern also found in our sample. Additionally, participants higher in depression and anxiety symptoms showed an opposing bias, which is in keeping with other studies linking MDD patients with slower reaction times to happy faces compared to healthy controls (see Weightman et al.'s (2014) review). Within our sample, however, the phenotypic correlations between happy RT and wellbeing (r=0.06) and happy RT and depression and anxiety symptoms (r=0.11) were small, and in the twin model, the only significant correlation with reaction time for happy faces was the genetic correlation with depression and anxiety symptoms (r=0.30). Previous studies suggest there may be common genetic influences between emotion processing of happy faces and mental health in the endocannabinoid system, for example the cannabinoid receptor 1 gene (CNR1; Chakrabarti & Baron-Cohen, 2011; Chakrabarti et al., 2006; Domschke et al., 2008;

Matsunaga et al., 2014). Variation in this gene has been shown to modulate activity in the striatum which is central to reward processing, specifically in response to happy faces in both healthy (Chakrabarti & Baron-Cohen, 2011; Chakrabarti et al., 2006) and clinically-depressed (Domschke et al., 2008) samples. In healthy individuals, allelic variation in four single-nucleotide polymorphisms (SNPs) of the CNR1 gene (the C allele in rs806377; G in rs806380; G in rs6454674; C in rs1049353) have been associated with higher striatal activity, a sensitivity for positive stimuli (i.e., happy faces) and, in the case of rs806377, higher levels of happiness (Chakrabarti & Baron-Cohen, 2011; Chakrabarti et al., 2006; Matsunaga et al., 2014). In clinically depressed individuals, genetic variation in the opposing G allele for the CNR1 SNP rs1049353 has been shown to confer risk for anxiety and depression, and antidepressant treatment resistance (Domschke et al., 2008). In the reported studies, genetic variation was specifically associated with emotion processing of happy faces and showed no effect in processing of disgust faces (Chakrabarti et al., 2006). The CNR1 gene is just one example of possible genetic variants that may underlie the common genetic associations identified here. In the current study, there was no genetic relationship between wellbeing and responses to happy faces; the significant genetic effect was specific to depression and anxiety symptoms. This finding highlights the independence of the wellbeing and depression and anxiety constructs, whereby despite showing a common phenotypic relationship with emotion processing of happy faces, the genetic underpinnings of these associations appear to be independent. This does not necessarily negate the potential for genetics to influence the relationship between wellbeing and emotion processing when measured using alternative behavioural (or other methodological) techniques. It would therefore be worthwhile to confirm this relationship in future research using alternative methodologies.

In other studies, inaccurate identification of neutral expressions has been identified in patients with Major Depressive Disorder (MDD) and anxiety disorders, for which they exhibit a bias

for inaccurately identifying neutral expressions in favour of threat-based emotions (Bar-Haim et al., 2007; Weightman et al., 2014). While we did not specifically examine the inaccurately identified emotion, our study identified an association between reduced accuracy to neutral faces and depressive symptoms in a healthy population. However, the phenotypic correlation was quite small, and in the twin bivariate model, neither environmental nor genetic correlations were significant. Our findings therefore suggest a minimal relationship between accuracy for neutral expressions and depressive symptoms within a healthy cohort. It is unclear why the phenotypic correlation was significant in the absence of significant genetic and environmental correlations. It may be that there is a third unmeasured variable mediating or moderating the relationship between depressive symptoms and neutral expressions, evident at the phenotypic level but not measurable in the twin model. For example, high trait neuroticism is a risk factor for depression and has been shown to be characterised by a negative information processing bias (Chan, Goodwin, & Harmer, 2007). It is plausible that accuracy for neutral expressions may relate to a misperception of neutral faces as a threat-based emotion, which would be consistent with a negative bias. Future studies could clarify this by including measures of the inaccurately identified emotion, and considering potential mediators/moderators such as neuroticism. The other main finding for wellbeing previously reported is associations between reduced wellbeing and increased negative emotion priming (Yu & Li, 2012), which was not supported in the current study. We found no relationship between explicit emotion identification or implicit emotion biases to negative emotions and wellbeing. One reason for this may be that these alterations are only seen in clinical samples with more pervasive languishing wellbeing scores. It would therefore be fruitful to confirm the current findings in another more clinically diverse population sample.

Our study also examined the univariate heritability for the different emotions within the emotion identification and bias tasks. For the emotion identification measures, the average

heritability was 34% for reaction time (range: 27-37%) and 24% (range: 23-28%) for accuracy. We consider the reaction time measures more reliable, however, due to the potential for ceiling effects in the accuracy measure. Across the sample, accuracy ranged from 48% for disgust faces to 92% for happy faces, and results were categorical rather than continuous, resulting in less sensitivity than the reaction time measures. These findings were consistent with previous heritability estimates of similar emotion identification measures, which ranged from 32% (Knowles et al., 2015) to 36% (Robinson et al., 2015). For the measures of emotion bias, the estimates were much lower: an average of 10% (range: 0-16%). A recent review (Gibb, McGeary, & Beevers, 2016) cites three twin studies investigating emotional attentional biases; however, one did not report heritability estimates, only (non-significant) genetic correlations (Brown et al., 2013); and the other two reported estimates for the heritability of EEG measures rather than behavioural responses (Anokhin, Golosheykin, & Heath, 2010; Weinberg, Venables, Proudfit, & Patrick, 2015). To our knowledge, our study is the first to report the heritability estimates for emotion bias (emotion minus neutral reaction times) measures in a twin sample. The reduced heritability for measures of emotion bias suggests unique environmental influences play a predominant role in implicit biases, accounting for 84-100% of the variance on bias scores. A range of environmental factors have been shown to influence emotion processing, as well as confer risk for depression, such as childhood maltreatment (Dannlowski et al., 2013), work-related burnout (Bianchi & Laurent, 2015), chronic pain (Apkarian et al., 2004) and substance dependence (Kornreich et al., 2003). Yet, negative attentional biases have been shown to be modifiable with cognitive training in meta-analyses (Beard, Sawyer, & Hofmann, 2012; Hakamata et al., 2010), indicating that explicit manipulation of emotion processing can alter implicit biases. These studies are just some examples of unique environmental factors that may influence the development and maintenance of emotional biases, and their alteration.

Together, our results suggest some small associations between wellbeing, depression and anxiety symptoms and specific emotional expressions. There are however several limitations of the current study. Being cross-sectional, this study cannot inform the causal direction of any relationship. A longitudinal design could inform the nature of these relationships, as well as the varying impact of genes and environment over time. Moreover, an intervention design would provide a better avenue for causal inference and allow for evaluation of gene-environment interactions. Given that environmental influences may have positive, negative or neutral effects, direct experimentation may be required to identify specific influences. Our sample was also quite healthy as a result of excluding participants with prior history of mental illness. It would therefore be useful to examine the covariance of normative variation in mental illness and mental wellbeing in a more heterogeneous population cohort to validate our findings. Finally, participation in this study was conducted remotely on participants' home or workplace computers. This was advantageous in terms of administration as it allowed twins to participate regardless of their location and schedule. We do however acknowledge the limitations of the design in that acquisition of information about the specific test-taking environment for each participant was beyond the scope of the study. However, the software supporting the behavioral assessment used in this study was designed to maximize control over testing parameters to the extent possible using remotely delivered assessments. For example, the software ensured that participants were required to complete the assessment in one setting and that they could not simultaneously use other applications (including web applications).

There are several future avenues whereby the current findings could be extended. For instance, the face emotion processing task used in the current study has been validated with demonstrated reliability, yet it is possible that future studies could consider the inclusion of other measures of emotion processing. For example, a recent paper by Wilhelm, Hildebrandt,

Manske, Schacht, and Sommer (2014) compiled a battery of 16 tasks comprehensively measuring facial emotion recognition and perception, including: images of faces with varying degrees of emotional intensity; composite faces with incongruent emotions; identification of emotions using dynamic faces; and emotion matching using faces from different viewpoints. A comprehensive measure of emotion processing such as this would be a valuable avenue for future research to avoid ceiling effects, and would also aid understanding of the neural circuitry recruited for emotion processing more specifically. In addition, it may also be useful to measure emotion processing using alternative measures to behavioural performance such as electroencephalography (EEG) or magnetic resonance imaging (MRI) techniques, which may show varied heritability than measures of behavioural reaction time. This would also provide the opportunity for investigation of dynamic emotion processing. Temporally dynamic tasks such as neutral expressions transitioning to an emotion with increasing intensity, for example, may show different or more extensive neural activation than static stimuli (Trautmann, Fehr, & Herrmann, 2009). Additionally, in this study we covaried for age and sex, yet other studies suggest that emotion processing is differentially impacted by both (Williams et al., 2009). Previous studies identifying relationships between emotion processing and wellbeing have mostly focused on young adults (Sanchez & Vazquez, 2014; Yu & Li, 2012), and it may be that our results differed from these studies as a result of the inclusion of a wider age bracket. It may therefore be valuable to examine the same associations in future studies but with a focus on age and sex differences. Finally, in this study we examined emotion biases in terms of speed of reaction time for correctly identifying facial expressions, yet another avenue for future research is to examine emotion biases in terms of the *inaccurate* identification of emotions. For example, in a review reported by Weightman et al. (2014), MDD patients often show a bias towards incorrectly identifying neutral faces as negative emotions. It would therefore be interesting to evaluate whether there

are any significant associations between variations in levels of wellbeing with incorrect emotional identification as there are with correct identification.

In conclusion, this study aimed to identify relationships between wellbeing, depression and anxiety symptoms and emotional function using emotion identification and implicit emotion bias tasks. An opposing association was found between reaction times to happy facial expressions, wellbeing scores and depression and anxiety scores, yet multivariate twin modelling identified a significant genetic correlation only with depression and anxiety symptoms. This highlights the independence of the wellbeing and depression and anxiety constructs. The size of the phenotypic associations was quite small. This may be partly due to the homogeneity of our sample. A further association between depression and anxiety symptoms and decreased accuracy for neutral expressions was also detected; however twin modelling identified no significant genetic or unique environmental correlations between the measures. Given the size of all identified relationships were small, it would be worthwhile to validate these associations in more heterogeneous samples in future research, and with other measures of emotion processing that may be more robust and/or have a stronger genetic influence.

Acknowledgements

This project was supported by an Australian Research Council (ARC) Linkage grant LP0883621, with Brain Resource Ltd as industry partner. This research was facilitated through Twins Research Australia which receives support from the National Health and Medical Research Council through a Centre of Research Excellence Grant, which is administered by the University of Melbourne. KMR is a PhD student supported by a NHMRC Postgraduate Public Health Scholarship 1055839. JMG is supported by a NHMRC Career Development Fellowship 1062495. PRS is supported by NHMRC Program Grant 1037196.

References

Anokhin, A. P., Golosheykin, S., & Heath, A. C. (2010). Heritability of Individual Differences in Cortical Processing of Facial Affect. *Behavior Genetics, 40*(2), 178-185. doi:10.1007/s10519-010-9337-1

Apkarian, A. V., Sosa, Y., Krauss, B. R., Thomas, P. S., Fredrickson, B. E., Levy, R. E., . . . Chialvo, D. R. (2004). Chronic pain patients are impaired on an emotional decision-making task. *Pain, 108*(1), 129-136. doi:10.1016/j.pain.2003.12.015

Bar-Haim, Y., Lamy, D., Pergamin, L., Bakermans-Kranenburg, M. J., & Van Ijzendoorn, M. H. (2007). Threat-related attentional bias in anxious and nonanxious individuals: a meta-analytic study. *Psychological Bulletin, 133*(1), 1.

Barkl, S., Lah, S., Harris, A. W. F., & Williams, L. M. (2014). Facial emotion identification in early-onset and first-episode psychosis: A systematic review with meta-analysis. *Schizophrenia Research, In press*.

Bartels, M. (2015). Genetics of Wellbeing and Its Components Satisfaction with Life, Happiness, and Quality of Life: A Review and Meta-analysis of Heritability Studies. *Behavior Genetics, 45*(2), 137-156. doi:10.1007/s10519-015-9713-y

Beard, C., Sawyer, A. T., & Hofmann, S. G. (2012). Efficacy of attention bias modification using threat and appetitive stimuli: a meta-analytic review. *Behavior therapy, 43*(4), 724-740. doi:10.1016/j.beth.2012.01.002

Bianchi, R., & Laurent, E. (2015). Emotional information processing in depression and burnout: an eye-tracking study. *European Archives of Psychiatry and Clinical Neuroscience, 265*(1), 27-34. doi:10.1007/s00406-014-0549-x

Boker, S. M. N., Michael C.; Maes, Hermine H.; Wilde, Michael J.; Spiegel, Michael; Brick, Timothy R.; Spies, Jeffrey; Estabrook, Ryne; Kenny, Sarah; Bates, Timothy C.;

Mehta, Paras; Fox, John. (2011). OpenMx: An open source extended structural equation modeling framework (Version 1.4): Psychometrika.

Brain Resource Ltd. (2010). *BRISC and WebNeuro Assessment Manual, v1.7* (B. R. L. Publishers Ed. Vol. 1.7). Sydney and San Francisco.

Brown, H. M., McAdams, T. A., Lester, K. J., Goodman, R., Clark, D. M., & Eley, T. C. (2013). Attentional threat avoidance and familial risk are independently associated with childhood anxiety disorders. *Journal of Child Psychology and Psychiatry, 54*(6), 678-685. doi:10.1111/jcpp.12024

Burton, K. L. O., Williams, L. M., Harris, A., Clark, C. R., Schofield, P. R., & Gatt, J. M. (2015). Sex differences in the shared genetics of dimensions of self-reported depression and anxiety. *Journal of Affective Disorders, 188*, 35-42. doi:10.1016/j.jad.2015.08.053

Chakrabarti, B., & Baron-Cohen, S. (2011). Variation in the human cannabinoid receptor CNR1 gene modulates gaze duration for happy faces. *Molecular Autism, 2*, 10-10. doi:10.1186/2040-2392-2-10

Chakrabarti, B., Kent, L., Suckling, J., Bullmore, E., & Baron-Cohen, S. (2006). Variations in the human cannabinoid receptor (CNR1) gene modulate striatal responses to happy faces. *European Journal of Neuroscience, 23*(7), 1944-1948.

Chan, S. W. Y., Goodwin, G. M., & Harmer, C. J. (2007). Highly neurotic never-depressed students have negative biases in information processing. *Psychological Medicine, 37*(9), 1281-1291. doi:10.1017/S0033291707000669

Damasio, A. R. (1994). *Descartes' error: emotion, reason and the human brain*. New York: G.P Putnam.

Dannlowski, U., Kugel, H., Huber, F., Stuhrmann, A., Redlich, R., Grotegerd, D., . . . Suslow, T. (2013). Childhood maltreatment is associated with an automatic negative

emotion processing bias in the amygdala. *Human Brain Mapping, 34*(11), 2899-2909. doi:10.1002/hbm.22112

Dillon, D. G., Rosso, I. M., Pechtel, P., Killgore, W. D. S., Rauch, S. L., & Pizzagalli, D. A. (2014). Peril and pleasure: An RDOC-inspired examination of threat responses and reward processing in anxiety and depression. *Depression and Anxiety, 31*(3), 233-249. doi:10.1002/da.22202

Domschke, K., Dannlowski, U., Ohrmann, P., Lawford, B., Bauer, J., Kugel, H., . . . Arolt, V. (2008). Cannabinoid receptor 1 (CNR1) gene: impact on antidepressant treatment response and emotion processing in major depression. *European Neuropsychopharmacology, 18*(10), 751-759.

Elliott, R., Zahn, R., Deakin, J. W., & Anderson, I. M. (2011). Affective cognition and its disruption in mood disorders. *Neuropsychopharmacology, 36*(1), 153-182.

Gatt, J. M., Burton, K. L. O., Schofield, P. R., Bryant, R. A., & Williams, L. M. (2014). The heritability of mental health and wellbeing defined using COMPAS-W, a new composite measure of wellbeing. *Psychiatry Research, 219*(1), 204-213. doi:10.1016/j.psychres.2014.04.033

Gatt, J. M., Korgaonkar, M. S., Schofield, P. R., Harris, A., Clark, C. R., Oakley, K. L., . . . Williams, L. M. (2012). The TWIN-E project in emotional wellbeing: study protocol and preliminary heritability results across four MRI and DTI measures. *Twin Research & Human Genetics: the Official Journal of the International Society for Twin Studies, 15*(3), 419-441. doi:10.1017/thg.2012.12

Gibb, B. E., McGeary, J. E., & Beevers, C. G. (2016). Attentional biases to emotional stimuli: Key components of the RDoC constructs of sustained threat and loss. *American Journal of Medical Genetics Part B: Neuropsychiatric Genetics, 171*(1), 65-80. doi:10.1002/ajmg.b.32383

Gomez, R., Summers, M., Summers, A., Wolf, A., & Summers, J. J. (2014). Depression Anxiety Stress Scales-21: Factor Structure and Test-Retest Invariance, and Temporal Stability and Uniqueness of Latent Factors in Older Adults. *Journal of Psychopathology and Behavioral Assessment, 36*(2), 308-317. doi:10.1007/s10862-013-9391-0

Gur, R. C., & Gur, R. E. (2016). Social cognition as an RDoC domain. *American Journal of Medical Genetics Part B: Neuropsychiatric Genetics, 171*(1), 132-141.

Gur, R. C., Sara, R., Hagendoorn, M., Marom, O., Hughett, P., Macy, L., . . . Gur, R. E. (2002). A method for obtaining 3-dimensional facial expressions and its standardization for use in neurocognitive studies. *Journal of Neuroscience Methods, 115*(2), 137-143. doi:http://dx.doi.org/10.1016/S0165-0270(02)00006-7

Hakamata, Y., Lissek, S., Bar-Haim, Y., Britton, J. C., Fox, N. A., Leibenluft, E., . . . Pine, D. S. (2010). Attention Bias Modification Treatment: A Meta-Analysis Toward the Establishment of Novel Treatment for Anxiety. *Biological Psychiatry, 68*(11), 982-990. doi:https://doi.org/10.1016/j.biopsych.2010.07.021

Keyes, C. L., Myers, J. M., & Kendler, K. S. (2010). The structure of the genetic and environmental influences on mental well-being. *American Journal of Public Health, 100*(12), 2379-2384. doi:10.2105/AJPH.2010.193615

Keyes, C. L. M. (2005). Mental illness and/or mental health? Investigating axioms of the complete state model of health. *Journal of Consulting & Clinical Psychology, 73*(3), 539-548.

Knowles, E. E., McKay, D. R., Kent Jr, J. W., Sprooten, E., Carless, M. A., Curran, J. E., . . . Olvera, R. L. (2015). Pleiotropic locus for emotion recognition and amygdala volume identified using univariate and bivariate linkage. *American Journal of Psychiatry, 172*(2), 190-199.

Kornreich, C., Foisy, M.-L., Philippot, P., Dan, B., Tecco, J., Noël, X., . . . Verbanck, P. (2003). Impaired emotional facial expression recognition in alcoholics, opiate dependence subjects, methadone maintained subjects and mixed alcohol-opiate antecedents subjects compared with normal controls. *Psychiatry Research, 119*(3), 251-260. doi:10.1016/S0165-1781(03)00130-6

Lovibond, P., & Lovibond, S. (1995). The structure of negative emotional states: Comparison of the Depression Anxiety Stress Scales (DASS) with the Beck Depression and Anxiety Inventories. *Behaviour Research and Therapy, 33*(3), 335-343. doi:10.1016/0005-7967-2894-2900075-U

Lovibond, P. F. (1998). Long-term stability of depression, anxiety, and stress syndromes. *Journal of Abnormal Psychology, 107*(3), 520-526. doi:http://dx.doi.org/10.1037/0021-843X.107.3.520

MacQueen, G. M. (2012). Systematic review of the neural basis of social cognition in patients with mood disorders. *Journal of psychiatry & neuroscience: JPN, 37*(3), 154.

Mathersul, D., Palmer, D. M., Gur, R. C., Gur, R. E., Cooper, N., Gordon, E., & Williams, L. M. (2009). Explicit identification and implicit recognition of facial emotions: II. Core domains and relationships with general cognition. *Journal of Clinical & Experimental Neuropsychology, 31*(3), 278-291. doi:10.1080/13803390802043619

Matsunaga, M., Isowa, T., Yamakawa, K., Fukuyama, S., Shinoda, J., Yamada, J., & Ohira, H. (2014). Genetic variations in the human cannabinoid receptor gene are associated with happiness. *PLoS ONE, 9*(4), e93771.

Paul, R., Lawrence, J., Williams, L. M., Clark, C. R., Cooper, N., & Gordon, E. (2005). Preliminary validity of "IntegNeuro": a new computerized battery of neurocognitive tests. *International Journal of Neuroscience, 115*(11), 1549-1567. doi:doi:10.1080/00207450590957890

R Core Team. (2013). R: A language and environment for statistical computing.

Robinson, E. B., Kirby, A., Ruparel, K., Yang, J., McGrath, L., Anttila, V., . . . Sleiman, P. M. (2015). The genetic architecture of pediatric cognitive abilities in the Philadelphia Neurodevelopmental Cohort. *Molecular Psychiatry, 20*(4), 454-458.

Routledge, K. M., Burton, K. L. O., Williams, L. M., Harris, A., Schofield, P. R., Clark, C. R., & Gatt, J. M. (2016). Shared versus distinct genetic contributions of mental wellbeing with depression and anxiety symptoms in healthy twins. *Psychiatry Research, 244*, 65-70. doi:10.1016/j.psychres.2016.07.016

Sanchez, A., & Vazquez, C. (2014). Looking at the eyes of happiness: Positive emotions mediate the influence of life satisfaction on attention to happy faces. *The Journal of Positive Psychology, 9*(5), 435-448. doi:10.1080/17439760.2014.910827

Silverstein, S. M., Berten, S., Olson, P., Paul, R., Willams, L. M., Cooper, N., & Gordon, E. (2007). Development and validation of a World-Wide-Web-based neurocognitive assessment battery: WebNeuro. *Behavior Research Methods, 39*(4), 940-949.

Sroufe, L. A. (1995). *Emotional Development: The organization of emotional life in the early years*. Cambridge: Cambridge University Press.

Trautmann, S. A., Fehr, T., & Herrmann, M. (2009). Emotions in motion: dynamic compared to static facial expressions of disgust and happiness reveal more widespread emotion-specific activations. *Brain Research, 1284*, 100-115.

Vittersø, J., Oelmann, H. I., & Wang, A. L. (2009). Life Satisfaction is not a Balanced Estimator of the Good Life: Evidence from Reaction Time Measures and Self-Reported Emotions. *Journal of Happiness Studies, 10*(1), 1-17. doi:10.1007/s10902-007-9058-1

Weightman, M. J., Air, T. M., & Baune, B. T. (2014). A review of the role of social cognition in major depressive disorder. *Frontiers in psychiatry, 5*, 179.

Weinberg, A., Venables, N. C., Proudfit, G. H., & Patrick, C. J. (2015). Heritability of the neural response to emotional pictures: evidence from ERPs in an adult twin sample. *Soc Cogn Affect Neurosci, 10*(3), 424-434. doi:10.1093/scan/nsu059

WHO. (1946). *Preamble to the Constitution of the World Health Organization as adopted by the International Health Conference, New York, 19-22 June, 1946; signed on 22 July 1946 by the representatives of 61 States (Official Records of the World Health Organization, no. 2, p. 100) and entered into force on 7 April 1948.*

Wilhelm, O., Hildebrandt, A., Manske, K., Schacht, A., & Sommer, W. (2014). Test battery for measuring the perception and recognition of facial expressions of emotion. *Frontiers in Psychology, 5*(404). doi:10.3389/fpsyg.2014.00404

Williams, L., Simms, E., Clark, C., Paul, R., Rowe, D., & Gordon, E. (2005). The test-retest reliability of a standardized neurocognitive and neurophysiological test battery:"neuromarker". *International Journal of Neuroscience, 115*(12), 1605-1630.

Williams, L. M., Gatt, J. M., Hatch, A., Palmer, D. M., Nagy, M., Rennie, C., . . . Paul, R. H. (2008). The integrate model of emotion, thinking and self regulation: an application to the "paradox of aging". *Journal of Integrative Neuroscience, 7*(3), 367-404.

Williams, L. M., Hermens, D. F., Palmer, D., Kohn, M., Clarke, S., Keage, H., . . . Gordon, E. (2008). Misinterpreting emotional expressions in attention-deficit/hyperactivity disorder: evidence for a neural marker and stimulant effects. *Biological Psychiatry, 63*(10), 917-926.

Williams, L. M., Mathersul, D., Palmer, D. M., Gur, R. C., Gur, R. E., & Gordon, E. (2009). Explicit identification and implicit recognition of facial emotions: I. Age effects in males and females across 10 decades. *Journal of Clinical & Experimental Neuropsychology, 31*(3), 257-277. doi:10.1080/13803390802255635

Yu, G.-M., & Li, B. (2012). How subjective well-being affects emotional processing: the role of event-related potentials. *Social Behavior and Personality: an international journal, 40*(8), 1285-1292.

Table 1. *Demographic characteristics of the current twin sample*

Variable	Total sample n=1668 (%)	Complete twin pairs n=1480 (%)
Total	1668	1480
Male	686 (41.1)	584 (39.5)
Female	982 (58.9)	896 (60.5)
MZ	1039 (62.3)	946 (63.9)
Male	472 (45.4)	420 (44.4)
Female	567 (54.6)	526 (55.6)
DZ	616 (36.9)	534 (36.1)
Male	204 (33.1)	164 (30.7)
Female	412 (66.9)	370 (69.3)
Unknown	13 (0.8)	-
Male	10 (76.9)	-
Female	3 (23.1)	-
Age (years, mean±SD)	39.65 ± 12.73	39.72 ± 12.76
Education (years, mean±SD)	14.35 ± 3.00	14.38 ± 2.97

Note. The total sample was used for the linear mixed models analyses. The complete twin pairs sample was used for the twin modelling.

Table 2. *Linear mixed model results for COMPAS-W wellbeing and DASS-42 total depression and anxiety scores predicting emotion scores in twin pairs*

Emotion Measure	COMPAS-W Wellbeing			Depression-Anxiety-Stress Scale		
	F	**β**	***p***	***F***	**β**	***p***
Emotion identification						
Angry RT†	1.840	0.000	0.18	0.264	0.004	0.61
Disgust RT†	1.373	0.000	0.24	0.001	0.000	0.97
Fear RT	2.051	-3.673	0.15	1.789	87.756	0.18
Happy RT†	***5.063***	***-0.001***	***0.02***	**6.748**	**0.015**	**0.01***
Sad RT†	2.810	-0.001	0.09	2.329	0.013	0.13
Neutral RT†	0.740	0.000	0.39	0.725	0.006	0.39
Angry % accuracy	0.053	-0.009	0.82	1.935	1.444	0.16
Disgust % accuracy	1.723	-0.055	0.19	0.070	0.286	0.79
Fear % accuracy	0.024	-0.007	0.88	0.288	-0.597	0.59
Happy % accuracy	0.003	0.000	0.95	1.082	0.230	0.30
Sad % accuracy	2.088	0.075	0.15	0.449	-0.899	0.50
Neutral % accuracy	1.919	0.044	0.17	**8.181**	**-2.334**	**0.00***
Implicit emotion bias						
Angry - Neutral RT	0.011	0.077	0.92	0.104	-6.160	0.75
Disgust - Neutral RT	1.515	0.920	0.22	0.257	-9.929	0.61
Fear - Neutral RT	0.440	0.493	0.51	0.014	-2.265	0.91
Happy - Neutral RT	0.920	0.743	0.34	0.666	-16.371	0.41
Sad - Neutral RT	1.667	1.015	0.20	0.153	-8.053	0.70

Note. RT, reaction time. Bolding indicates significant results at the adjusted *p* threshold for multiple comparisons ($p < .01$), bolding with italics indicating trend-level effects ($.01 < p < .05$). These analyses include both twins of each pair, controlling for family relatedness (twin 1, twin 2), zygosity (MZ, DZ), age, sex and education random variation. †log-transformed variables.

Table 3. *Univariate heritability and unique environmental estimates for emotion processing scores*

Emotion measure	a^2 (95% CI)	e^2 (95% CI)	Intra-class Correlations	
			MZ	**DZ**
Emotion identification				
Angry RT†	0.30 (0.22-0.37)	0.70 (0.63-0.78)	0.291**	0.255**
Disgust RT†	0.34 (0.27-0.41)	0.66 (0.59-0.73)	0.341**	0.235**
Fear RT	0.37 (0.30-0.44)	0.63 (0.56-0.70)	0.374**	0.189**
Happy RT†	0.27 (0.19-0.35)	0.73 (0.65-0.81)	0.272**	0.157**
Sad RT†	0.37 (0.30-0.44)	0.63 (0.56-0.70)	0.364**	0.260**
Neutral RT†	0.36 (0.29-0.44)	0.64 (0.56-0.71)	0.379**	0.141*
Angry % accuracy	0.28 (0.20-0.35)	0.72 (0.65-0.80)	0.257**	0.245**

Disgust % accuracy	0.23 (0.16-0.31)	0.77 (0.69-0.84)	0.216**	0.226**
Fear % accuracy^	0.00 (0.00-0.12)	0.77 (0.70-0.84)	0.191**	0.316**
Sad % accuracy	0.24 (0.17-0.32)	0.76 (0.68-0.83)	0.236**	0.195**
Neutral % accuracy	0.23 (0.15-0.31)	0.77 (0.69-0.85)	0.228**	0.118*
Implicit emotion bias				
Angry - Neutral RT^^	0.05 (0.00-0.14)	0.95 (0.86-1.00)	0.06	0.007
Disgust - Neutral RT	0.12 (0.04-0.20)	0.88 (0.80-0.96)	0.118**	0.092
Fear - Neutral RT	0.16 (0.07-0.24)	0.84 (0.76-0.93)	0.161**	0.075
Happy - Neutral RT	0.15 (0.07-0.23)	0.85 (0.77-0.93)	0.161**	0.061
Sad - Neutral RT^^	0.00 (0.00-0.07)	1.00 (0.93-1)	-0.018	-0.009

Note. Abbreviations: a^2, genetic (heritability) estimate; e^2, unique environment estimate; CI, confidence interval; RT, reaction time. ICC conducted as two-way mixed effects consistency model of single measures. *p<0.01; **p<0.001. † log-transformed variables. ^ACE model was best fitting, c^2 0.23 (0.12-0.30). ^^E model was best-fitting, but as it is unlikely there are zero genetic influences, parameters for AE model are included. Covariates in the models included age, sex and education.

Table 4. *Model fit statistics for multivariate genetic modelling of DASS-42 depression and anxiety, COMPAS-W Wellbeing and emotion processing scores*

Model	-2LL	*df*	AIC	diff LL	diff df	*p*	Compared to model
Model: Wellbeing, depression and anxiety symptoms, and RT for explicit identification of Happy faces							
AE CF model	9084.78	4413	258.78				
CF: sub 1	9148.94	4414	320.94	64.16	1	**0.00**	**No A corr, wellbeing and DASS**
CF: sub 2	9087.46	4414	259.46	2.68	1	0.10	No A corr, wellbeing and happy RT
CF: sub 3	9092.55	4414	264.55	7.77	1	**0.01**	**No A corr, DASS and happy RT**
CF: sub 4	9181.62	4414	353.62	96.84	1	**0.00**	**No E corr, wellbeing and DASS**
CF: sub 5	9084.93	4414	256.93	0.15	1	0.70	No E corr, wellbeing and happy RT
CF: sub 6	9085.35	4414	257.34	0.56	1	0.45	No E corr, DASS and happy RT
Model: Depression and anxiety symptoms, and accuracy for explicit identification of Neutral faces							
AE CF model	13115.91	2942	7231.913				
CF: sub 1	13116.19	2943	7230.189	0.28	1	0.60	No A corr, DASS and Neutral acc
CF: sub 2	13117.20	2943	7231.201	1.29	1	0.26	No E corr, DASS and Neutral acc

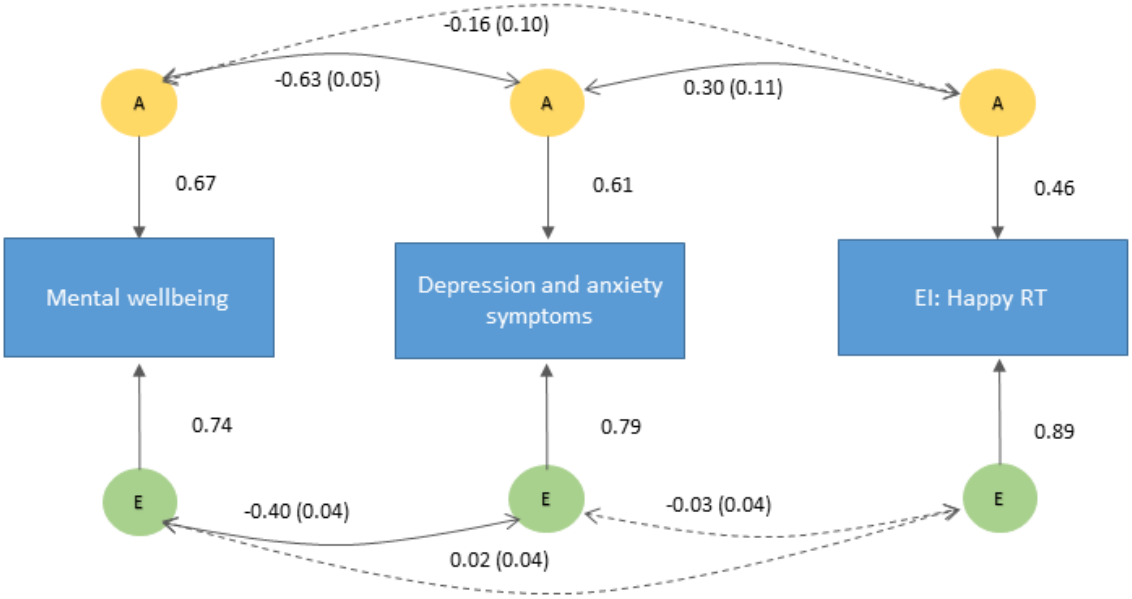
Note. Bolding indicates significant correlations. RT: reaction time; CF: correlated factors model; A: additive genetics; E: unique environment; DASS: Depression-Anxiety-Stress Scale; RT: reaction time. All models compared to the full AE CF model.

Figure Legend

Figure 1: Correlated-factors models for wellbeing, depression and anxiety symptoms and emotion processing scores.

FIGURE 1

(a).


-0.16 (0.10)
-0.63 (0.05)
0.30 (0.11)
A
A
A
0.67
0.61
0.46
Mental wellbeing
Depression and anxiety symptoms
EI: Happy RT
0.74
0.79
0.89
E
E
E
-0.40 (0.04)
-0.03 (0.04)
0.02 (0.04)

(b).

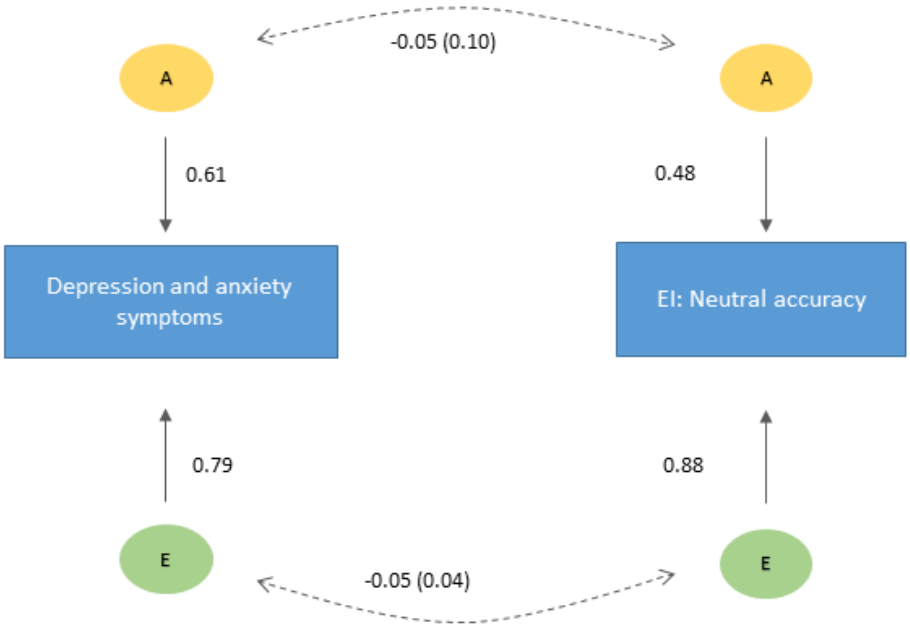

-0.05 (0.10)
A
A
0.61
0.48
Depression and anxiety symptoms
EI: Neutral accuracy
0.79
0.88
E
E
-0.05 (0.04)

Figure includes additive genetic (A) and unique environmental (E) influences on the phenotypes wellbeing, depression and anxiety symptoms and emotion identification variables. All path estimates are standardized. Single-headed arrows indicate the impact of the genetic and environmental factors on the phenotypes; double-headed arrows represent the genetic and environmental correlations between factors. Standard errors are in brackets, and dotted paths represent non-significant effects. *Figure 1a: Multivariate AE correlated-factors models for depression and anxiety symptoms, wellbeing and reaction time for identification of happy faces. Figure 1b: Bivariate AE correlated-factors models for depression and anxiety symptoms and accuracy for identifying neutral faces.*