1   **Title (120 characters maximum)**

2   Different aspects of social relationships contribute to subjective well-being via different

3   functional connectomes (109 characters)

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1   **Abstract**

2   The achievement of improved subjective well-being (SWB) is a worldwide issue. Prior studies

3   using self-report questionnaires have demonstrated that better social relationships (SR) form

4   the foundation for better SWB. To confirm the relationships with objective measure and

5   investigate the biological underpinning, we conducted connectome-based prediction modeling

6   with a 10-fold cross-validation, utilizing resting state functional magnetic resonance imaging

7   data ($n = 761$). Two aspects of SWB (life satisfaction and positive affect) were successfully

8   predicted using SR-related functional connections (FCs). The models also showed good

9   prediction performance in a validation sample ($n = 91$), suggesting that our models are

10   generalizable. All six aspects of SR considered were related to different sets of FCs with

11   minimal overlap in edge level. The contributions of these FC sets to the two aspects of SWB

12   were substantially different. In the future, effort should be made to improve all aspects of SR

13   to achieve better SWB. (149 out of 150 words)

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1   **Introduction**

2   Since the 1980s, the topic of subjective well-being (SWB) has received a lot of attention from

3   researchers, economists, and policy makers (Diener, 1984; Layard, 2010). Researchers

4   established that good SWB are protective against the well-known impacts of major life events,

5   and are related to a lower chance of physical and mental illness, as well as to increased

6   longevity (Diener & Chan, 2011; Luhmann, Hofmann, Eid, & Lucas, 2012; Wood & Joseph,

7   2010). Economic research has shown that average SWB increase as the nation average income

8   increases, contrary to the phenomenon known as "Easterlin Paradox" (Frank, 2012). However,

9   a survey by the Organization for Economic Co-operation and Development revealed a lack of

10   improvement in SWB in many of its member countries over the past decade, despite

11   improvements in income and health (OECD, 2017).

12   SWB is a complex cognition which has global impacts. Researchers have examined

13   how SWB consist and are associated with other social factors. One such factors is social

14   relationships (SR). SR refer to a social structure made up of relationships with a wide range of

15   people, including family members, neighbors, colleagues and peers, as well as emotional and

16   instrumental supports (Goswami, 2011). SR have both positive aspects, such as friendship,

17   emotional and instrumental supports, and negative aspects, such as perceptions of hostility,

18   loneliness, and rejection by peers. Prior studies have reported that better SR are the foundation

19   for better SWB (Siedlecki, Salthouse, Oishi, & Jeswani, 2014). However, such studies only

20   utilized self-report questionnaires to examine the relationships, leaving potential objective and

21   biological bases underlying the relationship between SR and SWB unexplored.

22   SWB have objective and biological correlates. Indeed, genetic research has shown that

23   genetic factors account for about one third of SWB (Bartels, 2015). A recent genome-wide

24   association study identified loci related to SWB (Okbay et al., 2016). Magnetic resonance

25   imaging (MRI) studies revealed the brain regions associated with SWB (Davidson & McEwen,

4

1   2012; Takeuchi et al., 2014), and SR also involve specific brain regions. For example, both

2   perceptions of hostility and rejection by peers are associated with functional connections (FCs)

3   related to emotional processing (Masten et al., 2011; Moses-Kolko et al., 2010), while

4   loneliness is associated with social brain regions (Kanai et al., 2012).

5   Given that relationships between SR and SWB were examined using only subjective

6   measures, confirming these relationships using objective measures, and investigating the

7   biological basis will deepen our understanding and provide a potential clue to improve SWB.

8   Prior studies have shown that both SR and SWB are associated with FCs and that SR lead SWB

9   (Davidson & McEwen, 2012; Masten et al., 2011; Siedlecki et al., 2014). Thus, we

10   hypothesized that SR have their neural correlates which underlie SWB. To address this

11   hypothesis, we analyzed resting-state functional MRI (R-fMRI) and phenotypic data collected

12   as a part of the Human Connectome Project (Van Essen et al., 2013).

13

14   **Results**

15   ***Prediction of SWB by models using FCs associated with SR***

16   After preprocessing the publicly available R-fMRI data, we obtained a 376×376 matrix based

17   on Glasser's atlas (Glasser et al., 2016), consisting of 360 cortical parcels and 16 subcortical

18   parcels, as regions of interest (ROIs). To examine whether SR have neural correlates that

19   underlie SWB, we used connectome-based prediction modeling (CPM) (Shen et al., 2017) with

20   a 10-fold cross-validation (CV). In this framework, we extracted FCs associated with SR and

21   then constructed models for predicting SWB using FCs associated SR. Fig. 1 shows an

22   overview of our analytical procedures and detailed procedures are described in Materials and

23   Methods. For clarity, we defined sets of FCs associated with SR as SR networks throughout

24   this manuscript.

1   Models with SR networks predicted two out of the three aspects of SWB: life

2   satisfaction ($r = 0.1202$, 95%CI = [0.0438, 0.1927], $P = 0.0009$); and positive affect ($r = 0.1086$,

3   95%CI = [0.0409, 0.1808], $P = 0.0027$), as shown in Fig. 2A. These results remained when

4   thresholds were set ($P < 0.001$, 0.005, and 0.05) for selecting relevant FCs (see Fig. S1).

5

6   ***Bootstrap analysis to test the associations between SWB and SR networks***

7   To examine whether SR networks were statistically significantly associated with SWB,

8   bootstrap analysis was performed. Prediction performances were compared with null models

9   that were built using randomly selected FCs not included in the pool of selected FCs in the

10   actual models (Yahata et al., 2016).

11   As shown in Fig. 2B, models with SR networks remained statistically significant for

12   life satisfaction ($P = 0.0004$) and positive affect ($P = 0.0008$), while mean and purpose did not

13   reach statistical significance ($P = 0.6948$). These results demonstrated that the prediction

14   performances of models with SR networks were indeed significant for the life satisfaction and

15   positive affect of SWB.

16

17   ***Generalizability of association between SWB and SR networks***

18   Model generalizability was tested using the validation dataset from "100 Unrelated Subjects."

19   As shown in Fig. 3, the models demonstrated statistically significant prediction accuracies for

20   both measures: life satisfaction: $r = 0.3951$, 95%CI = (0.2443, 0.5339), $P = 0.0001$; and positive

21   affect: $r = 0.4918$, 95%CI = (0.3313, 0.6204), $P < 0.0001$. These results further support the

22   association between the life satisfaction and positive affect of SWB, and SR networks.

23

24   ***Reproducible associations between FCs and SWB and SR***

6

1   To investigate whether the relationships of FCs with SWB and SR were reproducible across

2   datasets, we performed mass univariate analyses. Pearson correlation coefficients were

3   calculated between the strength of FCs and the degrees of SWB and SR for each dataset. As

4   shown in Fig. S2, the effects of SWB and SR on FCs over the two datasets were positively

5   correlated (all $r > 0.32$), suggesting that these effects are reproducible. Permutation tests with

6   5,000 iterations confirmed statistically significant positive correlations for SWB and SR (all P

7   < 0.001).

8   We next investigated whether relationships of SWB-FC and SR-FC were correlated in

9   both datasets. The Pearson correlation coefficients of SWB-FC and SR-FC were computed for

10   each FC. As shown in Fig. S3 and Fig. S4, statistically significant associations between life

11   satisfaction and positive affect of SWB and SR were observed in both datasets. These results

12   reflect the similarities in the SWB-FC and SR-FC relationships.

13

14   ***Associations between SWB and personality trait-related networks***

15   In addition to SR, personality traits may have influences on the extent of SWB (Kong, Hu,

16   Xue, Song, & Liu, 2015; Okbay et al., 2016; Strickhouser, Zell, & Krizan, 2017). To investigate

17   whether personality traits were also associated with SWB, we built prediction models with 10-

18   fold CV, replacing SR with personality traits. The models did not predict any of the measures

19   of SWB (all $P > 0.078$, after Bonferroni correction; Fig. S5). These results suggest that SR,

20   rather than personality traits, are associated with two aspects of SWB: life satisfaction and

21   positive affect.

22

23   ***Contributions of SR network to SWB***

24   To examine which SR networks contributed significantly to the prediction of life satisfaction

25   and positive affect, Wilcoxon signed rank tests were performed on the weight coefficients

1   obtained during 10-fold CV. The threshold for statistical significance was set to $P < 0.05$, with

2   Bonferroni correction for 12 comparisons.

3   Statistical analyses revealed that networks of positive SR, such as friendships and

4   instrumental supports, mainly contributed to prediction of life satisfaction (Fig. 4A), while

5   networks including aspects of loneliness, perceptions of hostility, and instrumental support

6   dominantly contributed to prediction of positive affect (Fig. 4B). These results suggest that

7   different SR networks are differently linked to life satisfaction and positive affect.

8

9   ***Network anatomy of SR networks***

10   Analyses were conducted to clarify the anatomy of SR networks. Binomial tests demonstrated

11   that each aspect of SR was associated with around 0.7%–1.3% of FCs in the whole brain

12   connections. In terms of positive aspects of SR (i.e., friendship, emotional support, and

13   instrumental support), networks exhibited similar trends, except for the instrumental support

14   network (Fig. 4C). For example, edges involved in the fronto-parietal (FP), somatomotor

15   (MOT), and dorsal attention (DAN) networks were more likely to be involved in networks of

16   friendship and emotional support. Edges stemming from limbic (Limb) and default mode

17   (DMN) networks were likely to be associated with instrumental support. In contrast, edges

18   from DMN and visual (Vis) networks were likely to be associated with negative aspects of SR

19   (Fig. 4D). These results indicate that each of the SR networks was substantially different.

20

21   ***Shared FCs within SR networks***

22   Since we obtained 12 SR networks, our conjunction analyses were restricted. Conjunction

23   analyses did not find any shared edges across the six SR networks for positive/positive,

24   negative/negative, positive/negative, or negative/positive combinations. As shown in Fig. 5A

25   and Table S3, networks of the positive aspects of SR (i.e., friendship, emotional support, and

8

1 instrumental support) shared only 10 positive edges and 6 negatives edges. Positive edges

2 consisted mainly of edges from the right insula and left precuneus to other regions, such as the

3 bilateral precentral gyri and the left inferior and middle temporal gyri, while negative edges

4 were from regions in DAN to other regions, such as the left inferior frontal gyrus and inferior

5 parietal lobule. In contrast, networks of the negative aspects of SR (i.e., loneliness, perceptions

6 of hostility, and perceptions of rejection by peers) contained eight positive edges mainly from

7 the DMN and Limb, and six negative edges stemming from regions in the Vis to other regions

8 involved in the DAN, DMN, and Limb (Fig. 5B and Table S3).

9

Discussion

11 The current study demonstrated that SR were associated with functional networks that were

12 eventually related to two aspects of SWB: life satisfaction and positive affect. More specifically,

13 life satisfaction was associated with all six aspects of SR, while positive affect was linked with

14 all, except for perceptions of rejection by peers. Although all aspects of SR were connected to

15 SWB, the degree of contribution of each differed. The neural bases were substantially different

16 from each other in edge level. These FC-SWB relationships were not reflected in personality

17 traits.

18 The R-fMRI data helped us disentangle the complexity of SWB. At the network level,

19 friendship and emotional support showed similarity in FCs in both positive and negative

20 directions. Given that the friendship and emotional support questionnaires ask about similar

21 aspects of social relationships, the similarity in the network patterns is understandable. FCs

22 negatively associated with friendship were positively associated with both life satisfaction and

23 positive affect, while FCs negatively associated with emotional support were negatively related

24 to life satisfaction and positive affect. These results may suggest that friendship may boost FCs

25 among some regions, while lack of emotional support leads to anti-correlation of activity

9

1 among some regions in the brain. Instrumental support had completely different FC networks

2 from those of friendship and emotional support, while it had the biggest effect on both life

3 satisfaction and positive affect. Although they were different, FCs negatively related to

4 loneliness and perception of hostility showed positive influence on both life satisfaction and

5 positive affect. FCs related to the perception of rejection by peers was negatively associated

6 with life satisfaction. These SR networks hardly overlapped in edge level. Such differences in

7 the way the SR-related FCs contributed to aspects of SWB and differences in edges that were

8 related to each aspect of SR may contribute to the complexity of SR-SWB relationships. Given

9 that all SR networks were shown to be related to at least one of the three aspects of SWB, the

10 current findings suggest that improvement in any of the SR parameters may lead to

11 improvements in SWB. These observations indicate that it is important to improve all the

12 aspects of SR to achieve better SWB.

13   The results of this study were in line with the results of prior studies that examined the

14 relationships between SR and SWB. However, meaning and purpose did not have any links

15 with any of the SR networks. There are two potential explanations for this discrepancy within

16 SWB. First, compared with life satisfaction and positive affect, meaning and purpose is a

17 product of higher order cognition, and consists of more complex combination of cognitive

18 components. Thus, SR networks were not related meaning and purpose. Another explanation

19 is that meaning and purpose can be inward and own feeling, which is independent from SR.

20 The lack of links between mean and purpose and SR networks suggests that this aspect of SWB

21 should be addressed differently from the other two aspects.

22   The current findings have some limitations. First, we used a cross-sectional dataset to

23 examine the triad associations between SWB, FC, and SR. Although we confirmed the main

24 findings using a validation dataset, the causal relationship among them is still unclear. Future

25 longitudinal investigations are necessary to elucidate the causal relationships. Second, although

1   we demonstrated associations between the SR and SWB, the types of SR that influence on

2   SWB may vary with developmental stages. For instance, relationships with parents might be a

3   critical factor from infancy to early adolescence (Chen, Haines, Charlton, & VanderWeele,

4   2019; Itahashi et al., 2019), while the influence of relationships with peers or other factors may

5   be pronounced in late adolescence to adulthood (Fortuin, van Geel, & Vedder, 2015). Future

6   research with subjects from multiple life stages (Harms et al., 2018; Somerville et al., 2018)

7   may help to further disentangle the complex associations between SWB and environmental

8   factors.

9   The current study corroborated the relationships between SR and SWB. Each aspect of

10   SR had a unique set of FCs, which was linked to at least one aspect of SWB. The current study

11   suggests the necessity of improving all the aspects of SR to achieve better SWB.

12

13   **Materials and Methods (less than 3000 words)**

14   ***Human Connectome Project dataset***

15   Data were collected as a part of the HCP (Van Essen et al., 2013). In this study, we used data

16   from the "1200 Subjects" public data release (https://www.humanconnectome.org/study/hcp-

17   young-adult) as a discovery dataset and those from the "100 Unrelated Subjects" set as a

18   validation dataset. The S1200 release and 100 Unrelated Subjects set originally contained 1113

19   subjects and 100 subjects, respectively. Our analyses were restricted to 763 subjects (397

20   females and 366 males) and 91 subjects (51 females and 40 males) who completed the NIH

21   toolbox (SR and psychological well-being) as well as personality traits, and who exhibited low

22   head motion during R-fMRI scans (< 3 mm translation, < 3° rotations, and < 0.15 mm in mean

23   FD).

24   The measures of psychological well-being obtained using the NIH toolbox, consisting

25   of general life satisfaction, meaning and purpose, and positive affect (Salsman et al., 2014).

26   We defined the psychological well-being as SWB because SWB usually include life

27   satisfaction and positive affect although the definition varies across studies (Diener, Suh, Lucas,

28   & Smith, 1999; Steptoe, Deaton, & Stone, 2015). SR evaluated in the project consisted of six

29   measures: friendship; loneliness; perceptions of hostility; and perception of rejection by peers

1 in daily social interactions; and emotional and instrumental support (Cyranowski et al., 2013).

2 Personality traits were assessed using the NEO-Five Factor Inventory (NEO-FFI) (McCrae &

3 Costa Jr, 2004). This contains 60 questions divided into five different personality domains with

4 12 questions for each, regarding: neuroticism; extraversion/introversion; openness to

5 experience; agreeableness; and conscientiousness. The details of the phenotypes are shown in

6 Table S1 and Table S2.

7

8 ***R-fMRI data preprocessing and network construction***

9 Minimally preprocessed R-fMRI data (Glasser et al., 2013) were obtained from the publicly

10 available HCP database. Using an in-house MATLAB code, we applied additional processing

11 procedures to the R-fMRI data, including the removal of the first 10 seconds of data for each

12 run, and nuisance regression on the data. Nuisance regressors consisted of linear detrending,

13 six head motion parameters, and averaged signals from the white matter, ventricles, and gray

14 matter, as well as their derivatives. A band-pass filter (0.008 - 0.1 Hz) was then applied to the

15 residuals. FD was calculated to identify motion-contaminated volumes (Power, Barnes, Snyder,

16 Schlaggar, & Petersen, 2012). To reduce spurious changes in FCs due to subtle head motion

17 during scans, a scrubbing method with 0.5 mm threshold of FD was applied, as described in a

18 previous study (Power et al., 2012).

19 We used Glasser's 376 surface-based brain regions (Glasser et al., 2016) as ROIs, to

20 characterize an individual's functional network. Pearson correlation coefficients were

21 calculated among all possible pairs of ROIs, yielding a 376×376 FC matrix for each subject.

22 Fisher's *r*-to-*z* transform was further applied to each correlation coefficient. These procedures

23 yielded 70,500 unique FCs, excluding the diagonal elements of the FC matrix. To facilitate the

24 interpretation of our findings, we identified the anatomical names of ROIs and the name of

25 resting-state networks (RSNs) using the automated anatomical labeling (AAL) (Tzourio-

26 Mazoyer et al., 2002) and a previous study (Yeo et al., 2011). We also added basal ganglia

27 (BG) network to the RSN labels.

1

2 ### *Connectome-based prediction modeling for SWB using FCs associated with SR*

3 We assumed that, if SR have their neural correlates which in turn underlie SWB, models using

4 FCs associated with FCs could predict the degree of the SWB. To test the association, we built

5 CPMs (Shen et al., 2017) with a 10-fold CV, for predicting SWB using SR networks. Fig. 1

6 shows an overview of our analytical procedures.

7 In each fold, we regressed out the effects of nuisance covariates, including sex, head

8 motion (mean FD), and the reconstruction version of fMRI (Dubois, Galdi, Paul, & Adolphs,

9 2018) from FCs, SWB, and SR. To identify FCs related to SR, Pearson correlation coefficients

10 were calculated between FCs and each measure of SR. The correlation coefficients were

11 thresholded at $P < 0.01$ (Rosenberg et al., 2016) and separated into a set of FCs positively

12 associated with SR and a set of those negatively associated with SR.

13 As a summary measure, connectivity strength (Rubinov & Sporns, 2010) was used to

14 characterize each participant's degree of FCs positively or negatively associated with each

15 measure of SR, resulting in 12 summary measures for SR; both positive and negative

16 associations with each of the six sub-scales of SR. We called these measures as "SR networks"

17 throughout this study. A multiple linear regression model with the SR networks was trained to

18 predict each measure of SWB. The trained model was used to predict the degree of SWB in the

19 left-out fold. Prediction performance was evaluated by calculating the Pearson correlation

20 coefficient between predicted and actual scores. The threshold for statistical significance was

21 set to $P < 0.05$ with Bonferroni correction (i.e., $P < 0.05/3 = 0.0167$).

22

23 ### *Bootstrap analysis to test associations SWB and SR networks*

24 Although analyses with the 10-fold CV found statistically significant associations between SR,

25 the brain, and parts of SWB (see **Results**), the possibility of "over-fitting" in the prediction

1   models remained (Whelan & Garavan, 2014). To examine whether SR networks were indeed

2   associated with SWB, bootstrap analysis was performed (Yahata et al., 2016), in which

3   prediction performances were compared with null models that were built using randomly

4   selected FCs not included in the pool of selected FCs in the actual models.

5   Using a bootstrap analysis with 5,000 iterations, the Pearson correlation coefficient of

6   the actual prediction models was compared with the null distribution derived from the bootstrap

7   procedure. Note that we selected a best prediction performance (i.e., highest correlation

8   coefficient) across all the null models at each iteration. The threshold for statistical significance

9   was set to $P < 0.05$.

10

11   ***Generalizability of association SWB and SR networks***

12   Although statistically significant associations were observed with 10-fold CV and bootstrap

13   analysis (see **Results**), the generalizability of observed associations remained. We tested the

14   generalizability of prediction models using the validation dataset ($n = 91$). We built a prediction

15   model using all the discovery dataset, with FCs selected during the 10-fold CV. Summary

16   measures were computed using FCs that were involved in SR networks at least one time during

17   the 10-fold CV procedure. The threshold for statistical significance was set to $P < 0.05$.

18

19   ***Characterization of the functional anatomy of edges***

20   To characterize the extent to which FCs contribute to the prediction, we performed

21   binomial tests (Yamagata et al., 2018). We selected a subset of FCs based on correlations with

22   each measure of SR in each fold. The feature selection procedure selected around 0.7 to 1.3%

23   of FCs in the whole brain connections across all the measures of SR in each of the 10 validation

24   folds. We assumed a binomial distribution with the probability of being selected from the set

1   of FCs. The threshold of statistical significance was set to $P < 0.05$ with Bonferroni correction

2   for 70,500 FCs with six measures of SR.

3   To further improve the interpretability of our findings, network anatomy was

4   determined with a hypergeometric cumulative density function (Lake et al., 2019). We

5   computed the probability of m significant edges in K possible edges in n edges from a finite

6   population of size M. The threshold of statistical significance was set to $P < 0.05$ with

7   Bonferroni correction for 36 comparisons. We also investigated the presence of shared edges

8   within SR networks by computing the element-wise product across networks.

9

Acknowledgments

17

Competing interests

19   All the authors declare that no competing interests exist.

20

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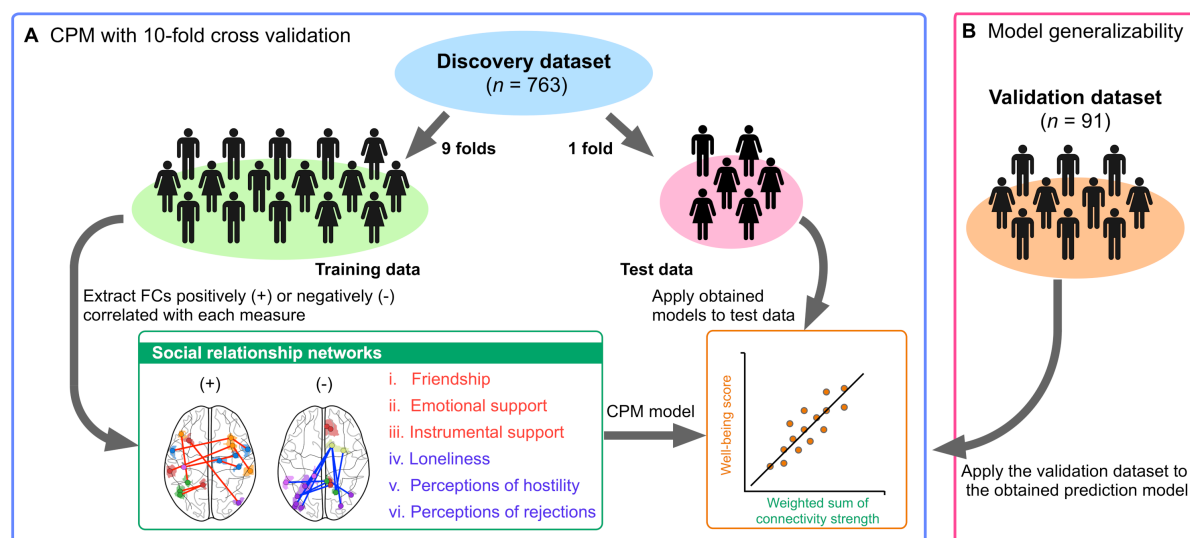
3 **Fig. 1. Schematic representation of the analytical procedures used in this study.**

4 Connectome-based predictive modeling (CPM) was performed using a 10-fold cross validation

5 (CV) in the discovery dataset ($n = 763$). The number of subjects was divided into 10 folds. At

6 each iteration, nine folds were used as a training data, to build models for predicting subjective

7 well-being (SWB) via functional connections (FCs) associated with social relationships (SR).

8 Pearson correlation coefficients were calculated between the strength of FCs and the degree of

9 SR. The set of correlations was thresholded ($P < 0.01$) to create feature sets that were either

10 positively (+) or negatively (-) correlated with SR. Then, the connectivity strength for each

11 measure of SR was computed for each subject in the training data. The sets of FCs associated

12 with SR were termed as "SR networks." Multiple linear regression was used to build a model

13 for predicting SWB from SR networks. The model was, then, applied to the left-out fold. The

14 predictive power was assessed by the Pearson correlation coefficient between predicted and

15 actual scores. Once statistically significant associations were observed, the model trained on

16 the whole discovery dataset was applied to the validation dataset ($n = 91$), to evaluate the model

17 generalizability.

18

A CPM results for SWB   **B** Results of bootstrap analysis

1
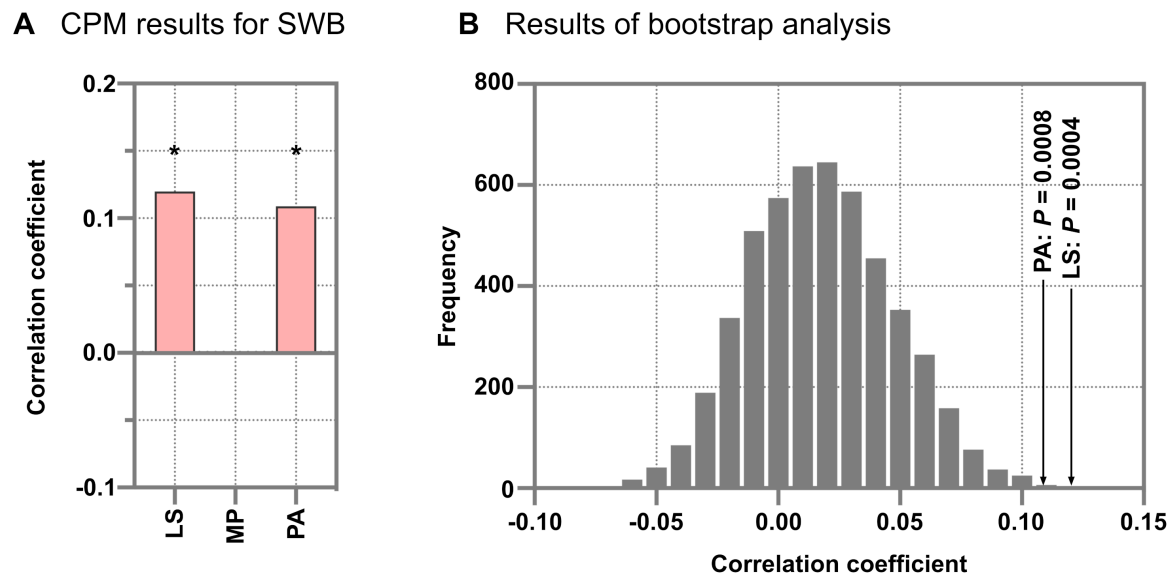
2   **Fig. 2. Performance of prediction models for subjective well-being using social**

3   **relationship networks.** (A) Bar graphs represent the prediction performances of the models

4   for subjective well-being (SWB). The asterisk denotes $P < 0.05$ with Bonferroni correction.

5   (B) The frequency of the different prediction performances is plotted in a bootstrap analysis

6   with 5,000 iterations. At each iteration, the same number of functional connections (FCs)

7   involved in social relationship (SR) networks was randomly selected from all 70,500 FCs

8   except for the FCs involved in the SR networks in the 10-fold cross validation procedure. The

9   highest correlation coefficients across all the null models were stored to construct the null

10   distribution. This analysis indicated that the probabilities of prediction performances of life

11   satisfaction ($r = 0.1202$) and positive affect ($r = 0.1086$) were small (life satisfaction: $P =$

12   0.0004 and positive affect: $P = 0.0008$), and demonstrated that SR networks were indeed

13   associated with SWB. **Abbreviations**: CPM: connectome-based predictive modeling, LS: life

14   satisfaction, MP: mean and purpose, and PA: positive affect.

15

21
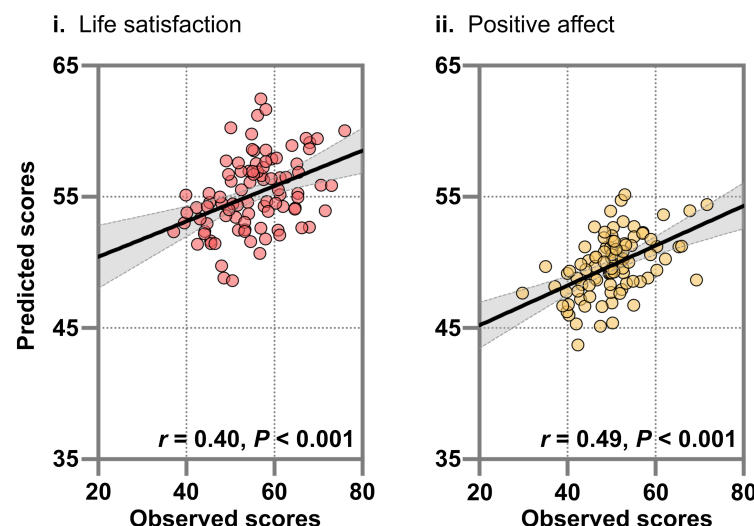
Fig. 3. Generalizability of social relationship networks for predicting life satisfaction and positive affect. Scatter plots show the prediction accuracies of constructed models for (*i*) life satisfaction and (*ii*) positive affect in the independent validation dataset ($n = 91$). Models were constructed using all the discovery dataset ($n = 763$) with functional connections selected at least once during 10-fold cross validation. These models were then applied to the validation dataset. Prediction performance was estimated by computing the Pearson correlation coefficient between observed and predicted scores. The threshold for statistical significance was set to $P < 0.05$.

Fig. 4. Anatomy of social relationships networks and contribution of these networks to the prediction of subjective well-being. Violin plots show the contribution of (A) positive and (B) negative networks to the prediction of life satisfaction (*i* and *iii*) and positive affect (*ii* and *iv*). The statistical significance of the contributions was assessed using the Wilcoxon signed rank tests. The asterisk represents the statistical significance after Bonferroni multiple comparison correction. For (C) positive and (D) negative social relationships, edge overlap (*i*

1   and *iii*) within and (*ii* and *iv*) between eight a priori networks (Yeo et al., 2011) and our social

2   relationship networks were plotted for sets of FCs (*i* and *ii*) positively and (*iii* and *iv*) negatively

3   associated with each measure of social relationships. Each layer plot shows the sum of

4   likelihood (1 - *P* value) estimated from the probability of edges shared between a priori

5   networks and each social relationship networks. In all the plots, within-network and between-

6   network pairs are sorted in the descending order. **Abbreviations**: BG: basal ganglia, DAN:

7   dorsal attention network, DMN: default mode network, ES: emotional support, FP: fronto-

8   parietal, Fri: friendship, HOSTILE: perceptions of hostility, IS: instrumental support, Limb:

9   limbic, LONELY: loneliness, MOT: somatomotor, REJECT: perceptions of rejections by peers,

10   VAN: ventral attention network, and Vis: visual.

11

A Edges shared across friendship, emotional support, and instrumental support
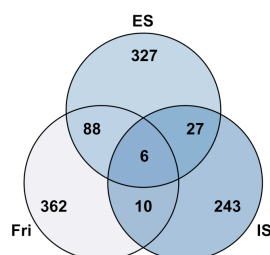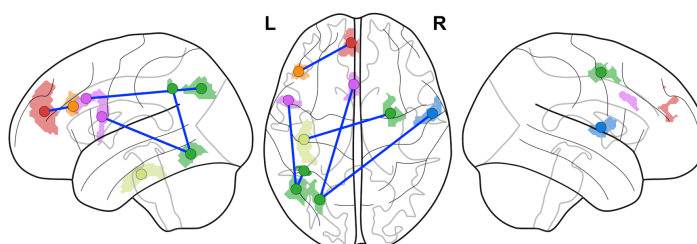
i. Venn diagram of shared edges (+)
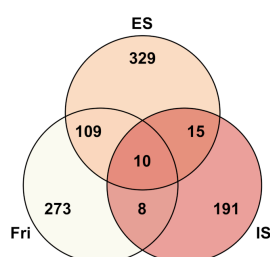
ii. Edges shared across friendship, emotional support, and instrumental support (+)
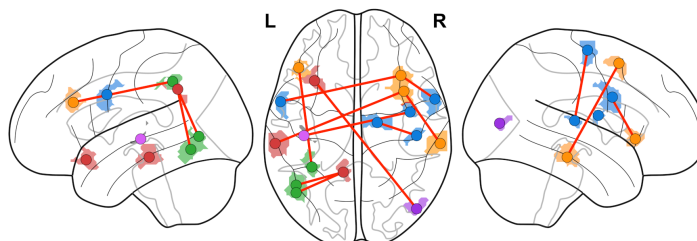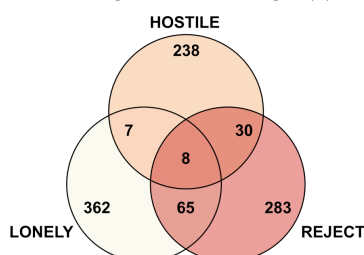
iii. Venn diagram of shared edges (-)

iv. Edges shared across friendship, emotional support, and instrumental support (-)
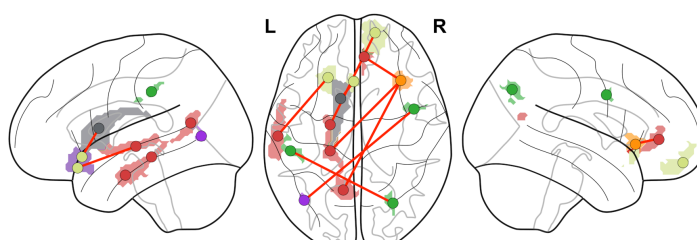
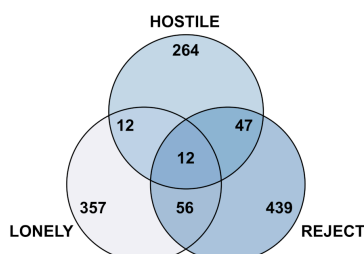**B** Edges shared across loneliness, perceptions of hostility, and perceptions of rejections

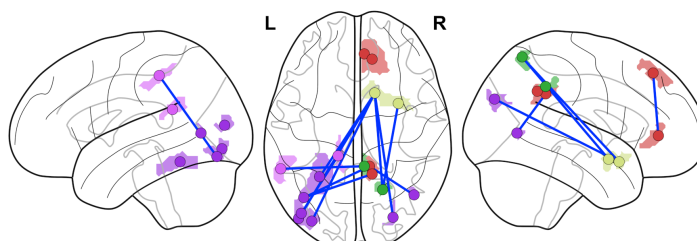**i.** Venn diagram of shared edges (+)

ii. Edges shared across loneliness, perceptions of hostility, and perceptions of rejections (+)

iii. Venn diagram of shared edges (-)

iv. Edges shared across loneliness, perceptions of hostility, and perceptions of rejections (-)

Visual (Vis) · Somatomotor (MOT) · Dorsal Attention (DAN) · Ventral Attention (VAN) · Limbic (Limb) · Fronto-parietal (FP) · Default (DMN) · Basal Ganglia (BG)

Fig. 5. Shared functional connections (FCs) across (A) positive and (B) negative social relationships. Venn diagrams represent the number of shared FCs (*i*) positively or (*iii*) negatively associated with each of (A) positive or (B) negative social relationships. (*ii* and *iv*) Distributions of shared FCs among all the three measures are visualized. **Abbreviations**: ES: emotional support, Fri: friendship, HOSTILE: perceptions of hostility, IS: instrumental support, L: left, LONELY: loneliness, R: right, and REJECT: perception of rejection by peers.

25

1   **Table S1. Phenotypic data of the discovery dataset**

	Male		Female		Statistics		
					t-statistics	*df*	*P*-value
# of samples	366		397		-	-	-
Subjective well-being							
Life satisfaction	54.52	8.61	55.92	9.12	-2.18	761	0.03
Mean and purpose	50.98	8.86	53.11	8.60	-3.37	761	<0.001
Positive affect	49.85	8.01	50.92	7.47	-1.90	761	0.06
Social relationship							
Friendship	50.48	9.09	50.73	9.04	-0.37	761	0.71
Emotional support	50.52	9.93	52.84	8.54	-3.47	761	<0.001
Instrumental support	47.84	9.46	48.35	8.36	-0.79	761	0.43
Loneliness	50.95	8.98	50.73	7.75	0.36	761	0.72
Perceptions of hostility	49.16	8.17	47.45	8.55	2.81	761	0.01
Perceptions of rejection by peers	48.57	8.93	47.65	8.46	1.46	761	0.14
Personality traits							
Neuroticism	15.80	7.76	17.05	6.60	-2.42	761	0.02
Extraversion	30.53	6.25	30.71	5.77	-0.42	761	0.67
Openness to experience	29.32	6.42	28.04	5.91	2.87	761	<0.01
Agreeableness	32.40	5.85	35.02	5.25	-6.51	761	<0.001
Conscientiousness	33.77	5.81	35.06	5.81	-3.08	761	<0.01

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3

1   **Table S2. Phenotypic data of the validation dataset**

	Male		Female		Statistics		
					t-statistics	df	P-value
# of samples	40		51		-	-	-
Subjective well-being							
Life satisfaction	55.62	8.62	55.20	8.55	0.23	89	0.82
Mean and purpose	51.89	8.94	52.34	8.77	-0.23	89	0.81
Positive affect	50.15	7.45	50.14	7.47	0.00	89	1.00
Social relationship							
Friendship	50.31	8.55	52.20	10.07	-0.95	89	0.35
Emotional support	50.27	10.22	52.65	9.58	-1.14	89	0.26
Instrumental support	51.16	9.76	48.54	7.59	1.44	89	0.15
Loneliness	49.69	9.14	51.11	8.37	-0.77	89	0.44
Perceptions of hostility	49.75	8.45	46.40	7.75	1.97	89	0.05
Perceptions of rejection by peers	47.93	8.39	47.93	8.69	-0.00	89	1.00
Personality traits							
Neuroticism	14.88	8.07	17.49	5.84	-1.79	89	0.08
Extraversion	29.98	6.07	30.96	6.09	-0.77	89	0.44
Openness to experience	28.55	6.06	27.51	5.99	0.82	89	0.42
Agreeableness	33.05	5.77	34.16	5.26	-0.95	89	0.34
Conscientiousness	35.35	4.70	35.18	5.40	0.16	89	0.87

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**Table S3. A list of functional connections (FCs) shared across social relationships.**

ROI1			ROI2			Type
Glasser's area name	AAL Label	Network	Glasser's area name	AAL Label	Network	
FCs shared across friendship, emotional support, and instrumental support						
R.AVI	Insula_R	FP	L.6v	Precentral_L	MOT	+
L.AIP	Parietal_Inf_L	DAN	L.p9-46v	Frontal_Inf_Tri_L	FP	+
R.LO3	Occipital_Mid_R	Vis	L.47s	Frontal_Inf_Orb_L	DMN	+
R.FOP2	Rolandic_Oper_R	MOT	L.52	Temporal_Sup_L	VAN	+
L.31pd	Precuneus_L	DMN	L.PH	Temporal_Inf_L	DAN	+
L.31pd	Precuneus_L	DMN	L.FST	Temporal_Mid_L	DAN	+
R.i6-8	Frontal_Mid_R	FP	L.TE1m	Temporal_Mid_L	DMN	+
R.6mp	Supp_Motor_Area_R	MOT	R.A1	Heschl_R	MOT	+
R.AVI	Insula_R	FP	R.6v	Precentral_R	MOT	+
R.TE1m	Temporal_Mid_R	FP	R.i6-8	Frontal_Mid_R	FP	+
L.IP1	Occipital_Mid_L	DAN	L.a24pr	Cingulum_Mid_L	VAN	-
L.p9-46v	Frontal_Inf_Tri_L	FP	L.9m	Frontal_Sup_Medial_L	DMN	-
L.PH	Temporal_Inf_L	DAN	L.6r	Frontal_Inf_Oper_L	VAN	-
R.6a	Frontal_Mid_R	DAN	L.TF	Temporal_Inf_L	Limb	-
L.IP2	Parietal_Inf_L	FP	L.PH	Temporal_Inf_L	DAN	-
R.43	Rolandic_Oper_R	MOT	L.IP1	Occipital_Mid_L	DAN	-
FCs shared across loneliness, perception of hostility, and perception of rejection by peers						
R.PEF	Precentral_R	DAN	L.MST	Occipital_Mid_L	Vis	+
R.AVI	Insula_R	FP	L.POS1	Precuneus_L	DMN	+
L.A5	Temporal_Mid_L	DMN	L.13l	Frontal_Inf_Orb_L	Limb	+
R.IPS1	Occipital_Sup_R	DAN	L.PFt	Parietal_Inf_L	DAN	+
R.10pp	Frontal_Sup_Orb_R	Limb	L.EC	ParaHippocampal_L	DMN	+

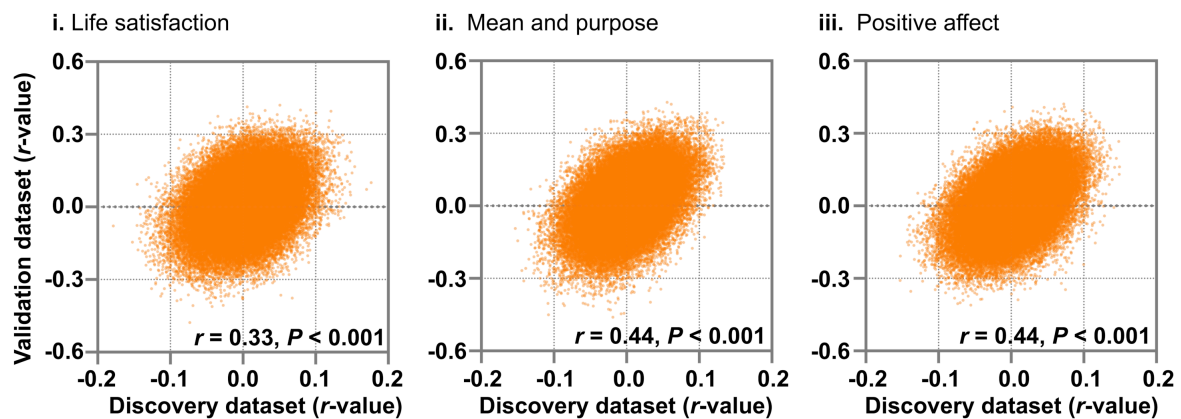|						
R.AVI	Insula_R	FP	L.PreS	ParaHippocampal_L	DMN	+
Left caudate	Caudate_L	BG	L.25	Olfactory_L	Limb	+
R.AVI	Insula_R	FP	R.a24	Cingulum_Ant_R	DMN	+
R.31pv	Cingulum_Mid_R	DMN	L.MST	Occipital_Mid_L	Vis	-
R.31pd	Precuneus_R	DMN	L.MST	Occipital_Mid_L	Vis	-
R.pOFC	Olfactory_R	Limb	L.LO2	Occipital_Inf_L	Vis	-
L.5mv	Cingulum_Mid_L	VAN	L.PIT	Fusiform_L	Vis	-
R.31a	Precuneus_R	FP	L.PSL	Temporal_Sup_L	VAN	-
R.pOFC	Olfactory_R	Limb	L.V3CD	Occipital_Mid_L	Vis	-
R.pOFC	Olfactory_R	Limb	L.VVC	-	Vis	-
R.31pv	Cingulum_Mid_R	DMN	R.MST	Temporal_Mid_R	Vis	-
R.pOFC	Olfactory_R	Limb	R.V7	Occipital_Sup_R	Vis	-
R.Pir	Insula_R	Limb	R.VIP	Parietal_Sup_R	DAN	-
R.pOFC	Olfactory_R	Limb	R.VIP	Parietal_Sup_R	DAN	-
R.8BL	Frontal_Sup_R	DMN	R.a24	Cingulum_Ant_R	DMN	-

Abbreviations: L: left, R: right, ROI: region of interest

Network: BG: basal ganglia, DAN: dorsal attention network, DMN: default-mode network, FP: fronto-parietal, Limb: limbic, MOT: somatomotor, VAN: ventral attention network, and Vis: visual.
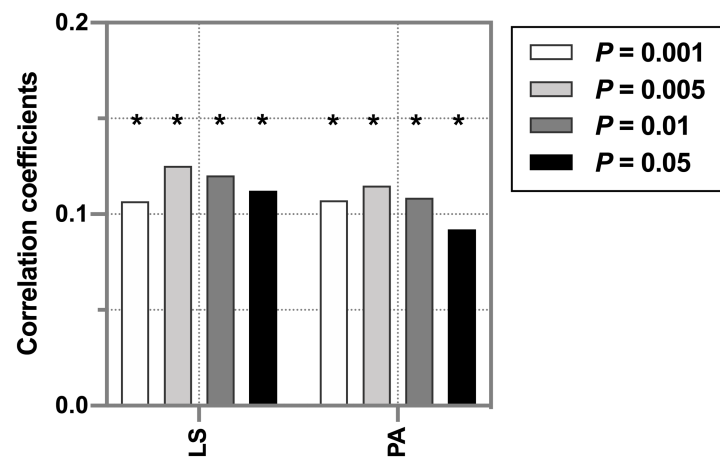
Fig. S1. Performance of prediction models for subjective well-being using social relationships networks with different thresholds. Bar graphs represent prediction performances with different thresholds. Four different thresholds ($P = 0.001$, 0.005, 0.01, and 0.05) were used for selecting functional connections (FCs) associated with the social relationships. The asterisks denote $P < 0.05$. **Abbreviations**: LS: life satisfaction, and PA: positive affect.

**A** Reproducible effects of subjective well-being on functional connections
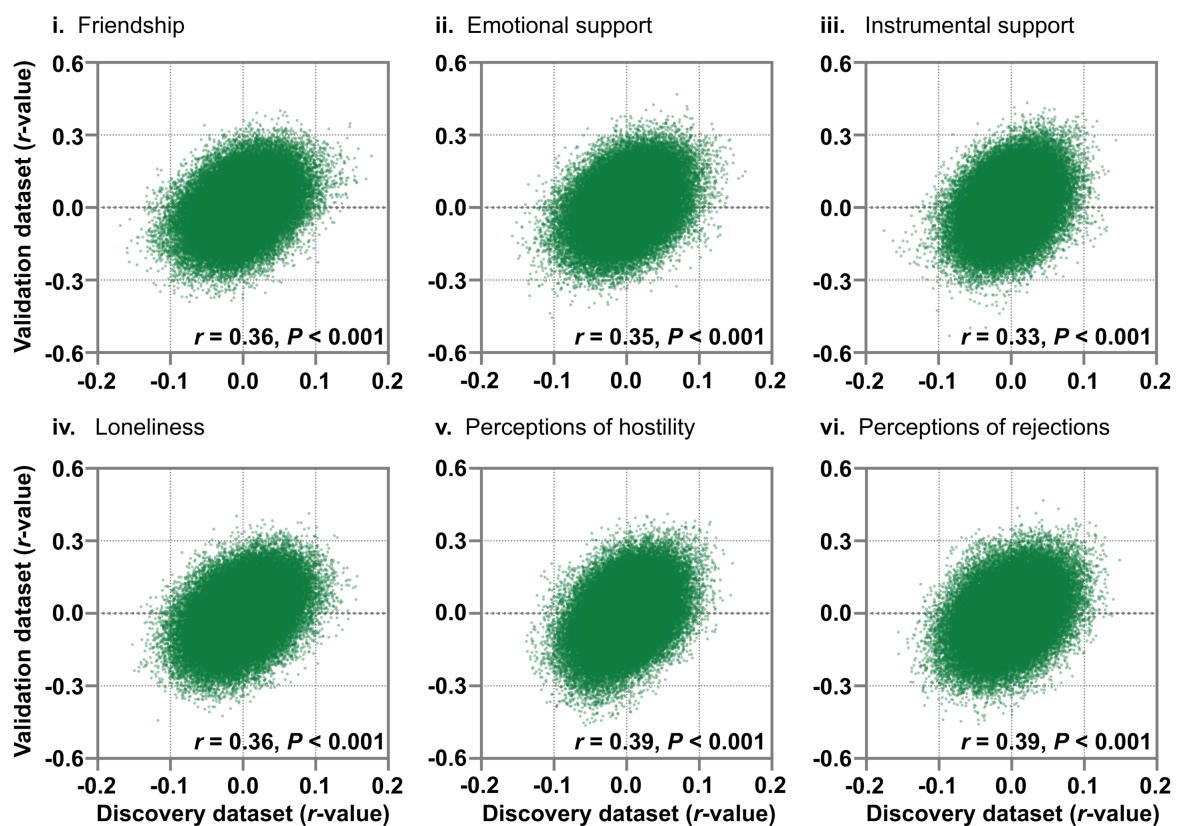
Fig. S2. Reproducible effects of subjective well-being (A) and social relationships (B) across datasets. Scatter plots represent associations between the discovery dataset and the validation dataset. Permutation tests with 5,000 iterations confirmed that the effects of subjective well-being and social relationships were reproducible (all $P < 0.001$).
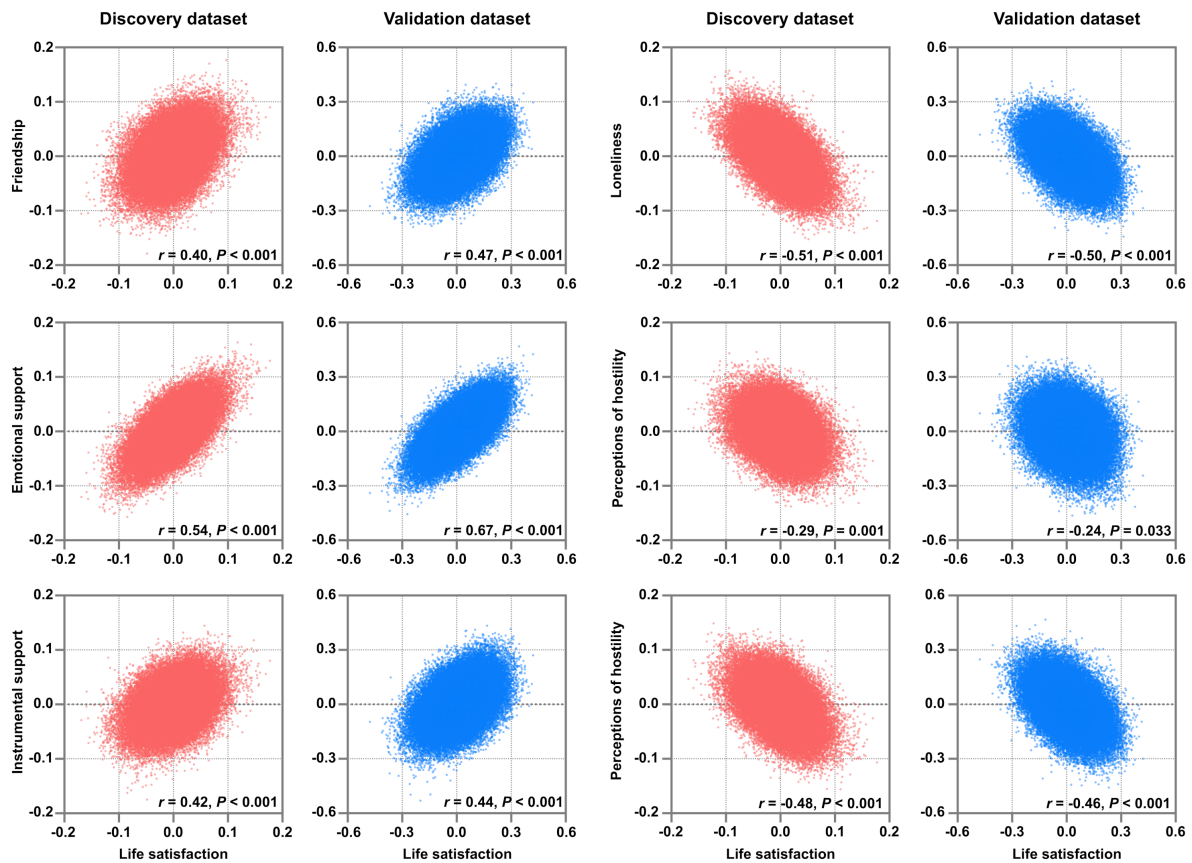
Fig. S3. Similarities in effects of life satisfaction and social relationships on functional connections. Scatter plots represent associations between life satisfaction and social relationships on functional connections (FCs) separately for discovery (red) and validation (blue) datasets. *P*-values were estimated using permutation tests with 5,000 iterations. The threshold for statistical significance was set at $P < 0.05$.
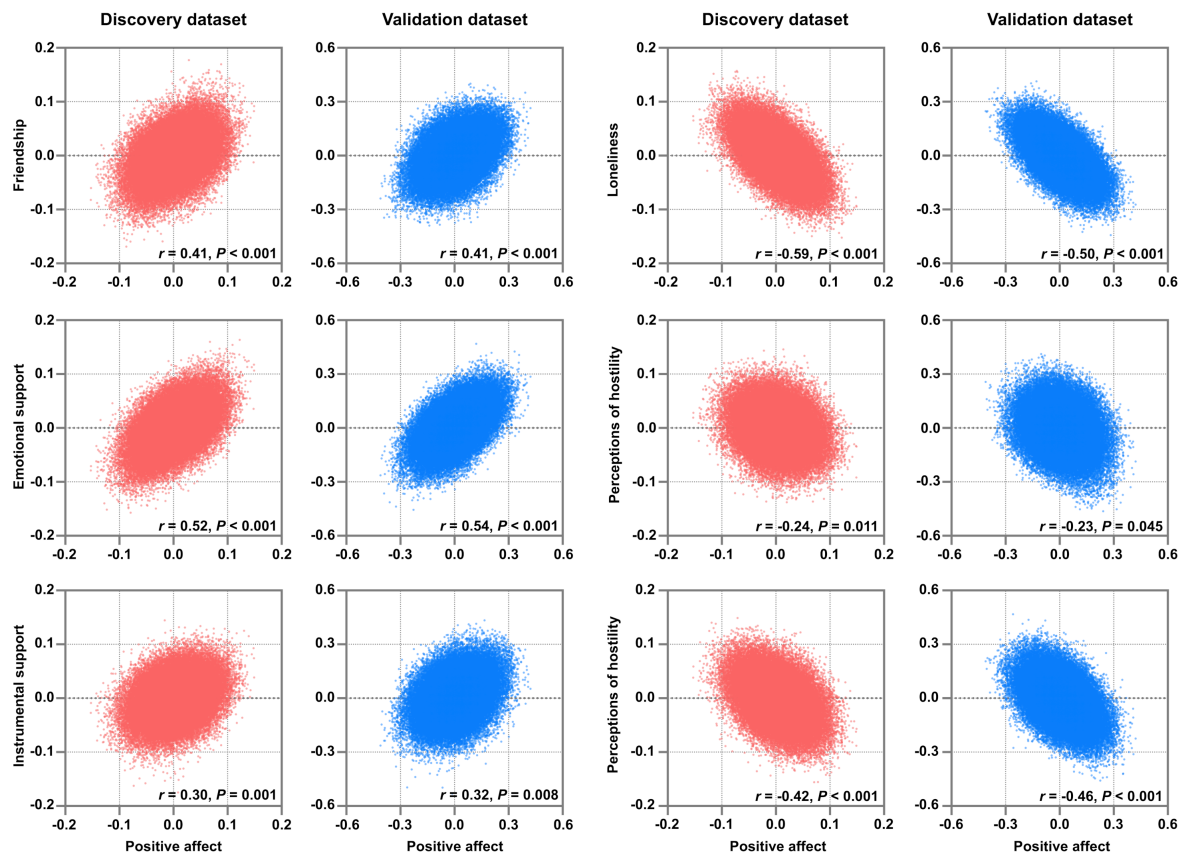
Fig. S4. Similarity in effects of positive affect and social relationships on functional connections. Scatter plots represent associations between the effects of positive affect and those of social relationships on functional connections (FCs) separately for discovery (red) and validation (blue) datasets. *P*-values were estimated using permutation tests with 5,000 iterations. The threshold for statistical significance was set at *P* < 0.05.

4
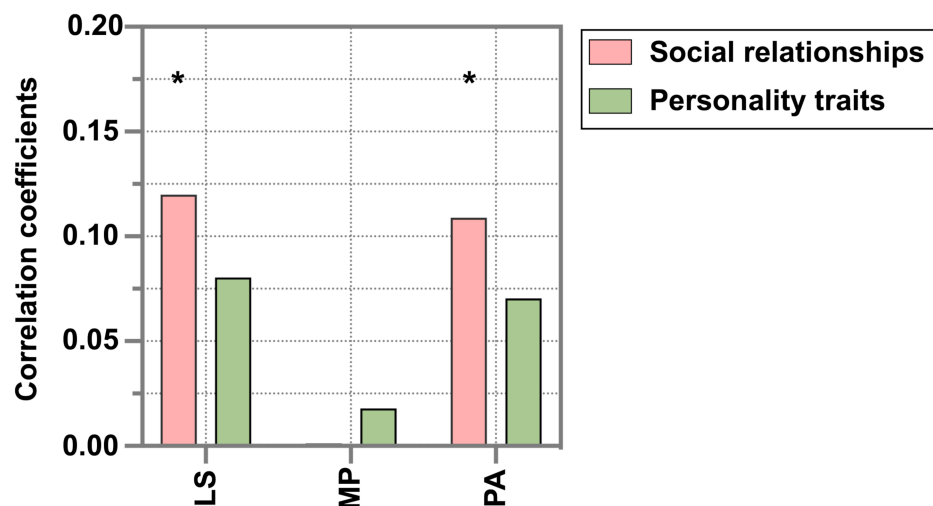
Fig. S5. Performance of prediction models for subjective well-being using social relationships and personality traits. Bar graphs represent correlation coefficients between observed and predicted scores using social relationships (pink) and personality traits (green). The asterisks indicate statistical significance (i.e., $P < 0.05/3$)