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Sociability and whole-brain resting-state connectivity

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Sociability is relevant for most mental health conditions and their prognosis. The classic "social brain" maps mainly to the default mode (DMN) and salience networks (SN). Recent studies also suggest involvement of other brain regions, but results are not yet fully consistent and interpretable. We conducted a fully data-driven resting-state connectivity study of sociability in the UK Biobank (*N* = 31,266). BOLD amplitude within, and timeseries correlations between 21 intrinsic brain networks were associated with a general sociability metric. Sociability showed modest but significant associations with many resting-state functional connectivity measures throughout the brain. Sociability was positively associated with sensorimotor network connectivity and showed intricate association patterns with SN and DMN connectivity. Based on our results, we hypothesise that there are important, probably reciprocal links between social behaviours and sensorimotor networks, and that social isolation may be accompanied by thought processes within the DMN being isolated from the rest of the brain.

Keywords Sociability, Resting-state functional magnetic resonance imaging (rs-fMRI), Functional connectivity, Default mode network (DMN), UK Biobank, Social isolation, Blood-oxygen-level-dependent (BOLD) imaging.

Sociability is a multifaceted construct, reflecting an individual's inclination to seek out and enjoy the company of others[1]. Sociability and its expression of social interaction are closely linked to mental health and psychiatric conditions. Low levels of sociability, expressed in e.g. loneliness and social withdrawal[2] are associated with a broad range of psychiatric conditions, including psychosis, autism spectrum, anxiety, and major depressive disorders[3–9]. Among persons with mental health problems, social isolation often precedes clinical diagnosis, and it predicts a more severe long-term trajectory; while a strong social network and more social activities are associated with positive long-term outcomes[7,8]. Sociability is thus an important transdiagnostic element and a possible modifiable factor that can improve wellbeing and aid in the prevention of, recuperation from, and (self-) management of mental health problems[2].

Neural systems that are relevant for sociability are distributed across the so-called "social brain"[10], consisting of regions associated with aspects of social behaviour, from attending to social cues and processing their valence to more complex functions like empathy[11]. Key regions of the "social brain" include the amygdala, orbitofrontal and medial prefrontal cortex (PFC), cingulate cortex, temporoparietal junction, anterior insula, and temporal pole[10,12–14]. These brain regions map onto the salience network (SN) and default mode network (DMN)[15–17]. The function and anatomy of many of the "social brain" regions, especially of medial PFC and insula, are amongst the most consistent brain patterns associated with psychiatric disorders, including major depression, bipolar disorder, and schizophrenia[14,18,19]. Sociability is thus a key transdiagnostic mental health trait that maps onto the neurobiological underpinnings shared by multiple mental health diagnoses.

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Measures of sociability can be categorised into two general constructs, which capture phenotypically and genetically correlated, yet significantly distinct aspects of sociability[3,20–22]: (1) objective measures of social activities, behaviours, and social networks and (2) measures reflecting more subjective experiences of social support, loneliness, and relationship satisfaction. Both types of sociability measures have been associated with increased functional activity and coupling within and between DMN and limbic networks, i.e. "internally focused" brain activation[21,23,24]. In addition, sensorimotor network connectivity has been reported in association with social behaviours and experiences, but the nature and patterns of these associations differed across studies[21,23,24].

Recently, both objective behavioural and subjective experience constructs of sociability have been linked with functional connectivity in the DMN in cohorts with major depressive disorder[25], schizophrenia, and Alzheimer's disease[20]. Irrespective of diagnosis, objective behavioural (i.e. few social activities, small social network) and subjective experiences (i.e. loneliness) of low sociability were associated with reduced functional connectivity of the DMN with the rostromedial PFC. A combined, additive metric of sociability capturing both subjective and objective measures was most sensitive to this association[20,25].

Most of these previous studies were however conducted in relatively small samples, which precluded fully data-driven whole-brain analyses and had limited power to detect more complex patterns of associations across the brain. The studies of brain function and sociability in larger samples were more data-driven, but were restricted to the cortex and based on atlas-based cortical parcellations[21,23,24]. Such approach excludes the subcortical hippocampus[26,27], amygdala[10,12–14], and ventral striatum[14,28], which are relevant for social processes and can be driving sources of functional brain organisation into canonical networks[29].

In the present study, we aimed to further investigate global patterns of brain connectivity and their association with sociability in a large population cohort, UK Biobank. Owing to the large sample size and fully data-driven whole-brain network-based analyses, including both cortical and subcortical regions and data-driven network definition, our results contribute to a more comprehensive neuroscientific understanding of what is typically considered "the social brain", in the general population and in those with mental health conditions.

Results

We analyzed resting-state fMRI data from 31,266 UK Biobank participants who also completed a four-item sociability sociability questionnaire, as in our previous studies[3,30]. Resting-state functional connectivity measures were based on independent component analysis as previously computed[31–34]. WIthin-network connectivity was was determined by blood-oxygen-level–dependent (BOLD) amplitudes as in[31,32]. Between-network connectivity was computed as pairwise full correlations between the average BOLD series of the 21 networks as in[31]. Associations between sociability scores and these connectivity metrics were assessed using Spearman partial correlations controlling for demographic, motion, brain volume, and imaging-site covariates, with false-discovery-rate correction applied to all tests.

The structure of this Results section follows the three-pronged approach we took in our analyses. First, we present the results from the main analysis: an exploratory and fully data-driven approach to map whole-brain functional connectivity patterns in association with sociability in the general population. Second, because of our consortium's previous findings specifically document rostromedial PFC and DMN connectivity in association with sociability[20,25], we follow with a confirmatory analysis that specifically focuses on these regions of interest within our results. Third, because our consortium's previous work indicated that sociability shows similar brain-connectivity associations across multiple mental health phenotypes, in a manner that is independent of (so not modulated by) diagnostic status, we here also present a supplementary analysis on whether our whole-brain results are similar in individuals with a mental health diagnosis compared to individuals without a mental health diagnosis.

Sociability is associated with functional connectivity within and between many brain networks

Correlations between sociability and between- and within- network functional connectivity measures are summarised in Fig. 1; Tables 1, 2 and 3, and Supplementary Table 1. Out of the 21 tests of within-network amplitudes correlations with sociability, 13 were significant after FDR correction. When separating the networks into "cognitive networks" (involved in higher-order cognitive and association processing) and sensorimotor networks (involved in perception and motor action), as defined in previous work[31,32,35] a notable pattern emerged: nine out of ten sensorimotor networks were associated with sociability. The direction of effect was positive in all cases. In contrast, within-network connectivity of only three cognitive networks showed a significant association with sociability, only one of which in a positive direction. This is also clearly apparent from Fig. 1, where somatosensory networks are depicted by the segments on the left with grey borders, and higher-order cognitive networks are on the right with black borders.

In the analyses of between-network connectivity, 99 out of 210 tests showed associations with sociability after FDR correction. Table 2 shows the top 20 between-network functional connectivity associations. The six strongest positive correlations were all between functionally similar and spatially proximal networks, such as between two language networks, or two sensorimotor networks. The seven strongest negative correlations all involved sensorimotor networks on the one hand, and their connection with anatomically and functionally distinct cognitive networks. Thus, sociability was associated with more integration of networks that are expected to be highly connected based on function and anatomical location, and with more segregation of the sensorimotor system from networks that are functionally and anatomically distal to the sensorimotor system. The between-network results are also illustrated in Fig. 1, represented by the chords connecting each of the outer segments.

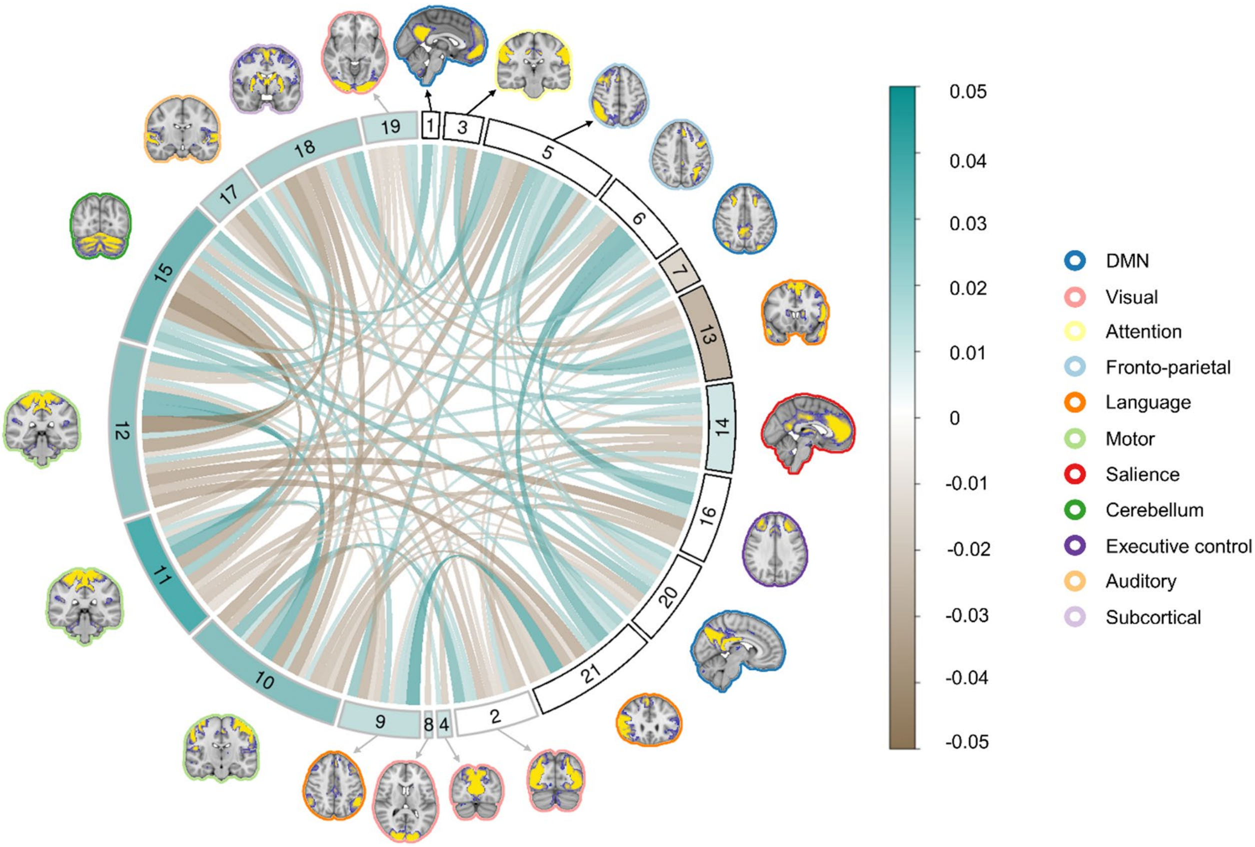

Fig. 1. Chord plot illustrating all associations between sociability and brain network connectivity. Numbered outer segments (1–21): Each numbered rectangle on the outer circle represents a distinct brain network, with its size reflecting the cumulative strength of correlations between sociability and the network's connectivity with other networks. Outer segment colours: Represent associations of sociability with within-network connectivity. Teal indicates positive associations (stronger connectivity in more sociable individuals), brown indicates negative associations, and white indicates statistically insignificant associations. Chords: The chords connecting the outer segments reflect the statistically significant between-network connectivity associations with sociability, again each chord's colour reflects of the strength of the correlation. Brain images: Illustrate the anatomical distribution of each network. Outer segment borders: Networks are organized with sensorimotor systems with grey border on the left and higher-order cognitive systems with black border on the right.

Network		Whole sample results		No mental health/psychiatric diagnosis		Mental health/psychiatric diagnosis		Diagnostic group comparison
Network name	Network number	Spearman Rho	*P* value (FDR-adjusted)	Spearman Rho	*P* value (FDR-adjusted)	Spearman Rho	*P* value (FDR-adjusted)	*P* value (FDR-adjusted)
Motor (2)	Network 11	0.0419	**2.63E-12**	0.0306	**4.2514E-04**	0.0537	**3.7813E-04**	0.9111
Cerebellum	Network 15	0.0376	**3.01E-10**	0.0293	**6.2326E-04**	0.0506	**5.5707E-04**	0.9111
Motor (1)	Network 10	0.0333	**2.62E-08**	0.0255	**0.0027**	0.0368	**0.0114**	0.9980
Language (2)	Network 13	−0.0323	**5.66E-08**	−0.0329	**0.0002**	−0.0317	**0.0314**	0.9980
Motor (3)	Network 12	0.0318	**8.17E-08**	0.0191	**0.0249**	0.0441	**0.0030**	0.9111
Subcortical	Network 18	0.0250	**3.56E-05**	0.0257	**0.0027**	0.0235	0.1150	0.9980
Auditory	Network 17	0.0225	**2.06E-04**	0.0231	**0.0068**	0.0419	**0.0043**	0.9111
Default Mode (2)	Network 07	−0.0187	**0.0025**	−0.0212	**0.0137**	−0.0203	0.1689	0.9980
Language (1)	Network 09	0.0175	**0.0045**	0.0202	**0.0178**	0.0129	0.4236	0.9980
Visual (4)	Network 19	0.0172	**0.0048**	0.0122	0.1700	0.0315	**0.0314**	0.9111
Visual (3)	Network 08	0.0145	**0.0198**	0.0060	0.4678	0.0382	**0.0097**	0.8567
Visual (2)	Network 04	0.0139	**0.0247**	0.0123	0.1700	0.0249	0.0988	0.9980
Salience	Network 14	0.0128	**0.0389**	0.0143	0.1156	0.0270	0.0719	0.9980

Table 1. Significant associations of sociability with within-network functional connectivity. Significant values are in bold.

Connectivity between			Whole sample results		No diagnosis		Mental health diagnosis		Comparison
Network names	Networks		Rho	*P* value (FDR-adjusted)	Rho	*P* value (FDR-adjusted)	Rho	*P* value (FDR-adjusted)	*P* value (FDR-adjusted)
Motor - CB	12	15	−0.044	2.05E-12	−0.038	5.07E-05	−0.053	0.0050	0.9490
Motor - Subc	12	18	−0.035	6.68E-08	−0.033	4.09E-04	−0.034	0.1125	0.9980
Motor - ExCon	12	16	−0.033	2.52E-07	−0.026	0.0044	−0.030	0.1653	0.9980
Motor - CB	10	15	−0.032	3.57E-07	−0.029	0.0013	−0.037	0.0724	0.9980
Motor - Lang	12	21	−0.031	9.05E-07	−0.023	0.0111	−0.028	0.1844	0.9980
Motor - Subc	10	18	−0.031	1.07E-06	−0.027	0.0028	−0.037	0.0724	0.9980
Motor - CB	11	15	−0.030	1.31E-06	−0.028	0.0025	−0.023	0.3127	0.9980
CB - Audit	15	17	−0.030	1.31E-06	−0.021	0.0236	−0.021	0.3712	0.9980
FP - Motor	5	10	−0.030	2.11E-06	−0.031	0.0010	−0.009	0.7554	0.9111
Att - FP	3	5	−0.027	1.49E-05	−0.033	0.0004	−0.004	0.9034	0.8644
Lang - Motor	9	10	−0.027	1.73E-05	−0.025	0.0062	−0.012	0.6678	0.9980
DMN - Motor	1	12	0.027	1.85E-05	0.021	0.0205	0.046	0.0226	0.9111
FP - CB	5	15	0.027	1.73E-05	0.020	0.0284	0.019	0.4271	0.9980
Visual - Motor	2	10	0.029	5.72E-06	0.029	0.0016	0.026	0.2446	0.9980
FP - Lang	5	13	0.030	1.59E-06	0.026	0.0039	0.044	0.0226	0.9190
FP - Lang	6	21	0.031	6.77E-07	0.029	0.0016	0.028	0.1927	0.9980
ExCon - FP	6	16	0.033	2.55E-07	0.035	0.0003	0.015	0.6153	0.9111
Motor - Motor	10	12	0.033	2.52E-07	0.031	0.0011	0.040	0.0535	0.9980
Motor - Motor	11	12	0.033	2.52E-07	0.032	7.16E-04	0.041	0.0407	0.9980
Lang - Lang	9	21	0.036	3.48E-08	0.042	3.56E-06	0.033	0.1297	0.9980

Table 2. The Twenty top significant associations of sociability with between-network functional connectivity. Motor, Sensorimotor; CB, Cerebellum; Subc, Subcortical; ExCon, Executive Control; Lang, Language; Audit, Auditory; FP, Frontoparietal; Att, Attention; DMN, Default-mode network.

Network name(s)	Network number(s)		Whole sample results		No diagnosis		Mental health diagnosis		Comparison
Within-network connectivity			Rho	*P* Value (FDR-adjusted)	Rho	*P* Value (FDR-adjusted)	Rho	*P* Value (FDR-adjusted)	*P* Value (FDR-adjusted)
DMN 1	1		0.003	0.5613	0.002	0.7632	0.001	0.9129	0.9979
DMN 2	7		−0.018	0.0024	−0.021	0.0137	−0.02	0.1688	0.9979
DMN 3	20		0.005	0.3819	0.008	0.3746	0.008	0.6323	0.9979
Salience	14		0.012	0.0389	0.014	0.1155	0.027	0.0718	0.9979
Between-network connectivity									
Sal–DMN 1	14	1	−0.01	0.1009	−0.014	0.1473	−8.1E-04	0.9765	0.9979
Sal–DMN 2	14	7	0.001	0.8862	0.002	0.7591	−0.001	0.9735	0.9979
Sal–DMN 3	14	20	0.017	0.0067	0.017	0.065	0.026	0.2276	0.9979
DMN 1–DMN 2	1	7	0.004	0.4716	0.006	0.5143	−0.001	0.9632	0.9979
DMN 1 – DMN 3	1	20	−0.012	0.0527	−0.018	0.0489	−0.004	0.8828	0.9979
DMN 2–DMN 3	7	20	−0.017	0.0068	−0.022	0.015	−0.012	0.6572	0.9979

Table 3. Associations of sociability with the within and between network functional connectivity for the default mode and salience networks.

Sociability associations with DMN and medial PFC connectivity

Guided by previous studies of DMN connectivity in relation to sociability[20,25], we performed an additional confirmatory analysis devoting special attention to connectivity patterns of the DMN and the rostromedial PFC. In our ICA-based network decomposition and categorisation[32], three networks were classified as DMN networks: a typical "core" DMN (network 1) and more limbic (network 7) and precuneal (network 20) DMN portions. Higher sociability was associated with reduced connectivity within the limbic DMN (Fig. 1, grey segment 7), and between the limbic DMN and the precuneal DMN (Fig. 1: grey chord connecting segments 7 and 20, Table 3). In contrast, higher sociability was associated with increased connectivity between each of the three DMN networks and frontoparietal networks (network 5 and/or 6), language networks (networks 9, 13, 21), and executive functioning network 16 (Supplementary Table 1).

Upon visual inspection, the map of the SN (network 14) also closely matched networks previously considered as DMN, and the previously reported rostromedial PFC region associated with sociability[20,25]. We found a positive association of sociability with connectivity within the SN (Fig. 1: outer segment 14, Table 1) and with connectivity between SN and precuneal DMN (Table 3; Fig. 1: teal chord connecting segments 14 and 20). Similar to the three DMN networks, SN-connectivity with several frontoparietal and language networks (networks 5, 9 and 21) was positively associated with sociability (Supplementary Table 1). In summary, higher sociability was most consistently linked with decreased intra-DMN connectivity, increased intra-SN connectivity, and increased connectivity of DMN and SN with higher-order cognitive networks.

Associations between sociability and brain connectivity by mental health status

Very similar patterns of brain-sociability associations were found in subgroups of individuals with and without a history of a broad spectrum of mental health diagnoses (Table 1). Effect sizes correlated strongly between the two groups (within-network: $r=0.85$, $p_{FDR}=8.66*10^{-7}$; between-network: $r=0.65$, $p_{FDR}=2.20*10^{-26}$; Supplementary Table 2). There were no significant group differences in the sociability-connectivity associations for any of the networks (all $p_{FDR} > 0.91$).

Discussion

We investigated resting-state functional brain networks in relation to sociability. Our findings indicate that sociability is associated with subtle, global patterns of both within- and between-network connectivity. Our findings are consistent with the previously reported role of the DMN and rostromedial PFC in social functioning and loneliness[20,25]. With our data-driven approach we show that brain regions relevant for social behaviour also extend far beyond the DMN and the classic 'social brain'[10,12–14]. We found a consistent pattern of positive association between sociability and connectivity within sensorimotor networks. All effect sizes were small, as expected[36]. Our hypothesis-generating analysis contributes to a more complete characterisation of brain areas relevant for social behaviour, and provides a basis for future, more detailed studies on the roles of different networks in social behaviours and preferences.

A first notable observation is the consistently (relatively) strongest, positive associations between sensorimotor network connectivity and sociability. Associations between sensorimotor network activation and social behaviour, loneliness, and perceived social support have been found previously in UKB[21,23,24]. However, previous findings were less straightforward to interpret due to finer-grained atlas-based methods and mixed directions of effects. Here, we used a global network-based approach that is fully determined by intrinsic voxel-wise covariance patterns of this sample, and we interpreted the networks according to our previously used classification system of sensorimotor networks and cognitive networks[31,32,35]. Owing to this, we see a clear pattern: nine out of ten sensorimotor networks showed increased within-network connectivity in association with higher sociability. In addition, sociability was associated with increased synchronisation between functionally similar and anatomically proximal networks, and with increased segregation of functionally or anatomically distinct networks.

Our study design was purely observational: we show how inter-individual variations in brain co-activation patterns relate to inter-individual variation in the degree and experience of daily social interactions. The co-activation patterns we identified can therefore be essential for seeking and positively valuing social interactions - as is known for the DMN and SN[14]. Lower sociability could also be a consequence of atypical somatosensory connectivity, e.g. less efficient sensory processing may make social interactions more difficult or less desirable. This hypothesis has been proposed to potentially explain social behaviour in autism[37,38], and is supported by recent experiments in mouse models[39]. However, the observed brain patterns can also be a consequence of social activities and experiences. Individuals who interact more often and more intensely with other people on a daily basis tend to perceive more diverse stimuli and be more physically active, resulting in increased co-activation of sensorimotor brain regions, effects which with synaptic plasticity can persist into the resting state[40,41]. A reasonable hypothesis is thus that people who generally interact more with the external world activate more sensorimotor regions on a daily basis, leading to lasting and habitually stronger functional integration of sensorimotor networks. Both complementary hypotheses require further (experimental) research. Both are consistent with our observations that sociability is associated with increased *integration within* sensorimotor networks and increased *segregation between* sensorimotor regions networks and higher order cognitive networks.

We also found modest but intricate associations with DMN and SN connectivity, as hypothesised. We found that higher sociability is associated with reduced connectivity within and between multiple DMN subdivisions. This seems contradictory to a previous finding[20,25] of reduced within-DMN connectivity in association with loneliness and social isolation. Yet, their finding was driven by the rostromedial PFC, which in our network definition[32] mapped to the SN. Indeed, we found increased SN-DMN connectivity in association with higher sociability. The relevant area in the rostromedial PFC, corresponding to Brodmann areas 10 and 32, is thought to be involved in the most complex forms of emotional processing: mentalising other's intentions and mental states, and further, in knowing other people's representations of our own intentions, deceptions, and mental states[13]. Together, our study thus contributes to strong converging evidence - from foundational neuroscience[13,14], observational studies[20,25] and genetic studies[30] - that reduced connectivity of rostromedial PFC with (other) DMN regions is associated with social isolation and loneliness.

Higher sociability was also associated with higher connectivity of the DMN and SN with task-positive cognitive networks such as executive control and language networks. The DMN is the signature network that is active during rest, mind wandering, and introspection[15]. An intriguing hypothetical interpretation is that, as people are more socially isolated, their own internal thought processes are also more isolated from the rest of the brain, and from other cognitive functions such as attention, executive control, and language. The SN, and in particular the rostromedial PFC region discussed above, is thought to act as a "switch" between DMN and task-positive functions[17]. Therefore, less co-activation of SN with both DMN and executive control networks could lead to more functional segregation of the DMN. Our hypothetical interpretation is that social isolation means DMN isolation: less connectivity with other people corresponds to less DMN-connectivity with the rest of the brain, which speculatively, corresponds to isolation of the internal thought and emotional processes from other forms of cognition.

Sociability and social isolation are important for mental health, and predictors of long-term outcomes for patients with mental health disorders. Previous research in the UK Biobank has shown that our sociability measure, comprised of a combination of social activity and subjective feelings of loneliness, is reduced in those with a diagnosis of schizophrenia, major depression, bipolar disorder, and autism spectrum disorder[3]. With this same sociability measure, we here identified patterns of brain network activation that are similarly important for sociability in the neurotypical population as for individuals with mental health conditions. This secondary analysis was aimed to test the generalisability of the brain-sociability association patterns observed in the total sample. By combining all psychiatric diagnoses in a single subgroup, we can indeed conclude that overall brain-sociability associations generalise, but we cannot directly infer whether one or more smaller diagnostic subgroups may also recruit distinct sociability-associated brain regions. Nevertheless, our data-driven results support previous findings of the transdiagnostic nature of key neural systems for sociability for depression, schizophrenia, Alzhemier's disease and undiagnosed individuals[20,25], and we provide new insights into their neural extent and complexity. Our results provide a basis for future hypothesis-driven clinically relevant investigations that can be conducted in smaller, more homogeneous, and (ideally) longitudinal clinical cohorts. For example, our new research points to the sensorimotor networks as relevant for social isolation, whether as a consequence or as a cause. In addition, above we explain how our results inspire the hypothesis that altered SN connectivity contributes to isolation of one's personal DMN "internal thought world" from other cognitive processes and from the external world, a mechanism that could be central to social isolation and the experience of loneliness. This is intriguing yet speculative, and clearly the causal role of the SN and DMN patterns in social isolation, in the emotional consequences of loneliness, and associated mental health problems need further investigation. Our results encourage a more targeted hypothesis-testing investigation of these brain systems in prospective functional MRI studies, ideally also combined with behavioural experimental designs and/or medial PFC neuromodulation[42].

Our fully data-driven whole-brain study is only possible with a very large sample size, such as provided by UKB. However, the UKB sample originates from one country, with an overrepresentation of higher socio-economic status. Therefore, important variation endemic to different parts of the world, different socio-cultural and socio-economic contexts is missed[43–45]. Another important characteristic of UKB is the lower bound on the age of the participants, with the youngest being in their forties, while sociability changes throughout the lifespan[46]. Finally, we emphasise that it is all effect sizes we observed are small, in line with expectations[36], and their significance is only visible at the population level, in samples of thousands of individuals.

Unlike previous data-driven functional connectivity studies of sociability in UKB[21,23,24], our network-based analysis included subcortical and cortical regions. Subcortical regions, including the amygdala and ventral striatum, are highly relevant for social processing[10,12–14,26–28]. Excluding subcortical activation profiles from network-based analysis has a major impact on the observed network topology and connectivity measures[29]. This explains why we detect stronger involvement of the limbic part of the DMN and the SN than those previous studies, as these networks are strongly driven by striatum and medial temporal lobe. Another difference between our approach and previous studies is that our network definition was fully driven by intrinsic voxel-wise patterns of co-activation using ICA rather than defined by atlases[21,23,24] or seed regions[20,25]. This resulted in different network topographies: for example, our SN was less driven by insula and more by medial PFC, and our DMN was subdivided into three networks. These methodological choices have advantages in terms of power and data-driven qualities, but they limit one-to-one comparison of our results with those previous results. Finally, we took a more global approach to network connectivity, which yielded a clear global pattern contrasting sensorimotor networks with cognitive networks, as inspired by[31,32,35], but limited the anatomical granularity.

No gold standard measure of sociability is currently available[1], which means that studies setting out to investigate sociability diverge in the construct they eventually measure, some of which are more quantitative and some more experiential[1]. Our metric of choice was constrained to questions already available in UKB, and it has been successfully used in the past[3]. However, it captures the broad and multifaceted construct in a single measure, without distinguishing between different facets of sociability.

Conclusion

In conclusion, this study revealed associations of inter-individual differences in sociability with subtle but widespread patterns of functional connectivity throughout brain, indicating that sociability is intricately linked to a broad array of neuronal systems. The strongest associations with sociability were found within the sensorimotor system. Further, our findings support a known key-role of the rostromedial PFC, SN, and DMN, and inspire a hypothesis on the dynamics of the SN and DMN with the rest of the brain. Our findings encourage more detailed investigations on the causal nature of these different brain associations with social behaviour, feelings of social belonging, and the possible consequences for mental health.

Methods

Data source: UK Biobank

UK Biobank (UKB)[47] is a large-scale multi-centre initiative within the United Kingdom established with the aim of contributing to the scientific efforts within the biomedical fields, currently containing data from over half a million participants phenotyped across multiple modalities. Our analyses were limited to a subset of the sample with both sociability measures and neuroimaging data available, based on scans from the first imaging visit and consisted of n = 31,266 participants for the analysis of functional amplitudes and n = 31,256 for the between-network connectivity analyses. Demographic information can be found in Supplementary Tables 3 and 4. Data were obtained under UKB application number 23,668.

Operationalisation of sociability

The sociability score was based on four questions: (1) How often do you visit friends or family or have them visit you?; (2) Which of the following do you attend once a week or more often? (multiple choice: sports club or gym, pub or social club, religious group, adult educational class, other group activity); (3) Do you worry too long after an embarrassing experience?; (4) Do you often feel lonely? The scores from the four questions were summed to calculate a composite sociability score, which was previously shown to be significantly heritable and associated with several psychiatric conditions in UKB[3]. For more information about the score, see Supplementary Methods and Figure S22. This score was not normally distributed. Therefore, Spearman's correlations were used for all statistics concerning this measure.

Resting-state functional magnetic resonance imaging measures

We used resting-state functional connectivity measures previously derived by the UKB brain imaging team[33,34] (Data-Fields 25754 and 25750). Acquisition, pre-processing, quality control, and analytic procedures have been described previously[33,34]. In brief, resting-state data were acquired on Siemens Skyra 3 T scanners in 3 data collection sites using the same protocols and hardware. Participants were scanned for 6 min, at 2.4-mm isotropic resolution, TR = 0.735s. Individual-level preprocessing included corrections for motion and distortions, high-pass filtering, and cleaning by applying the automatic "FIX" algorithm in FSL. Group ICA analysis was carried out using FSL MELODIC[48] at two dimensions 25 and 100. Here, we choose the 25-dimensional solution since it reduces the multiple testing burden and has previously been well validated in terms of biophysical properties and sensitivity to lifestyle and demographic variables[32]. Among the 25 spatial ICA maps, 4 were identified as artifact-related (e.g. motion, non-neural physiological properties, or scanner distortions), based on visual inspection[32,34]. For the remaining 21 non-artifact components, 21 individual-level within-network connectivity measures and 210 pairwise between-network connectivity measures were obtained as previously[31,32,35]. Within-network connectivity was measured by blood-oxygen-level dependent (BOLD) amplitude, computed as the within-component standard deviation of the BOLD signal. BOLD amplitude has been shown to be primarily originate from the temporal synchrony of the voxels, thus effectively capturing functional connectivity[32]. Between-network connectivity was computed more traditionally, as the pairwise full correlations between the 21 components. A visual illustration of the component-based networks, and their network names consistent with[32], can be found in the Supplementary Figures S1–S21 and online (https://www.fmrib.ox.ac.uk/ukbiobank/group_means/rfMRI_ICA_d25_good_nodes.html).

Statistical analysis

Spearman's correlation coefficients were calculated between the sociability score and within- and between-network connectivity measures. We controlled for confounding effects of sex, age, head motion (framewise displacement), total brain volume, and data-collection site using partial correlations.

To investigate whether patterns of brain activation were associated with sociability irrespective of psychiatric diagnoses, we repeated the above analyses in two subgroups: individuals with and without a record of psychiatric diagnoses (UKB Data Field 29000). Individuals without responses were excluded from this analysis. Since our previous results showed very similar patterns of brain-sociability associations across multiple diagnostic categories[20,25], and given the very variable and sometimes relatively small sample sizes for certain diagnostic categories (e.g. $n = 241$ for ADHD, $n = 7{,}808$ for panic attacks), we grouped all diagnoses together for the purpose of this generalisability test. We compared the Spearman's correlations between the diagnosed and undiagnosed subgroups by Fisher's Z-transforming the correlation coefficients, subtracting the resultant Z-scores between the groups, followed by a Z-test relative to its standard error. We also tested the similarity of the connectivity-sociability associations between both groups, using Pearson's correlations of the Fisher-transformed network-sociability associations across networks.

All the analyses were performed in R version 4.1.0 (https://www.r-project.org/). To correct for multiple comparisons, the false-discovery rate (FDR) was estimated using the Benjamini-Hochberg method[49].

Data availability

All data used in this article are available through the UK Biobank (https://www.ukbiobank.ac.uk/).

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Author contributions

Conceptual design: CF, MJHK, AS, BF- Data processing and analysis: MR, ES, Il, AFM, GF- Results presentation and interpretation: MR, ES- Manuscript draft: MR, ES- Manuscript revision: MR, ES, II, GF, AFM, CF, MJHK, AS, BF.

Declarations

Competing interests

BF has received educational speaking fees and travel support from Medice GmbH. MJHK has received educational speaking fees and travel support from Angelini and Boehringer Ingelheim. AS is or has been a consultant to or has received honoraria or grants unrelated to the present work from: Abbott, Abbvie, Angelini, Astra Zeneca, Clinical Data, Boheringer, Bristol Myers Squibb, Eli Lilly, GlaxoSmithKline, Innovapharma, Italfarmaco, Janssen, Lundbeck, Naurex, Pfizer, Polifarma, Sanofi, Servier, Taliaz. The other authors do not report any potential conflicts of interest.

Additional information

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