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Heterogeneous factors influence social cognition across diverse settings in brain health and age-related diseases

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Aging diminishes social cognition, and changes in this capacity can indicate brain diseases. However, the relative contribution of age, diagnosis and brain reserve to social cognition, especially among older adults and in global settings, remains unclear when considering other factors. Here, using a computational approach, we combined predictors of social cognition from a diverse sample of 1,063 older adults across nine countries. Emotion recognition, mentalizing and overall social cognition were predicted via support vector regressions from various factors, including diagnosis (subjective cognitive complaints, mild cognitive impairment, Alzheimer's disease and behavioral variant frontotemporal dementia), demographics, cognition/executive function, brain reserve and motion artifacts from functional magnetic resonance imaging recordings. Higher cognitive/executive functions and education ranked among the top predictors, outweighing age, diagnosis and brain reserve. Network connectivity did not show predictive values. The results challenge traditional interpretations of age-related decline, patient–control differences and brain associations of social cognition, emphasizing the importance of heterogeneous factors.

Social cognition plays a key role in human interaction, encompassing the mental processes involved in perceiving, interpreting and responding to the social cues of others[1]. The core and most studied components are emotion recognition and mentalizing[2]. Emotion recognition conveys the ability to identify how others feel. Mentalizing is the capacity to infer the mental states of others, such as their intentions, beliefs and desires. Aging may diminish performance in both processes[3], associated with gray matter loss and functional connectivity changes across brain networks[4,5]. Social cognition dysfunction in aging can increase social isolation, loneliness and vulnerability[6], impacting brain health[7] and quality of life[8]. Standardized tasks of social cognition are increasingly used in research and clinical contexts to assess the performance of patients with age-related conditions such as subjective cognitive complaints (SCC), mild cognitive impairment (MCI) and dementia, in comparison to that of healthy controls (HCs)[9–11]. However, despite its relevance, several gaps persist in our understanding of the factors that influence social cognition in aging.

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One critical problem is the considerable variability observed in social cognition performance among otherwise similar individuals[12], especially in the older population[3] and at a global scale[13,14]. This variability may stem from multiple factors, such as demographic characteristics (sex, age, education[13–16] and socioeconomic status[17,18]) and individual differences in other cognitive abilities (for example, memory and processing speed[4]) or executive functions (for example, inhibition and working memory[19]). Brain reserve, defined as the accumulation during the lifespan of structural and functional brain resources that mitigate the effects of neural decline caused by aging or disease[20], may also play a role in social cognition variability[4,5]. Crucially, when considering underrepresented aging samples from low- and upper-middle-income countries (UMICs), brain health determinants exhibit greater heterogeneity, challenging mainstream evidence from high-income countries (HICs)[21–25]. Socioeconomic disparities worsen brain health and increase the rate of dementia[23]. Within these heterogeneous determinants, factors related to disparities, such as social determinants of health and education can exert a stronger influence than traditional factors such as age and sex[21]. Thus, heterogeneity constrains standard brain–behavior and brain–phenotype associations[26–30], and predictive models often fail to classify individuals with nonstereotypical profiles regarding demographics, clinical presentation, admixtures, cognition and brain function[26,27]. In the same vein, functional connectivity-based models usually fail to generalize to diverse samples and are influenced by image acquisition artifacts, particularly in-scanner head motion[26,31,32]. These issues limit our ability to draw generalized conclusions about social cognition in healthy and pathological aging, hampering the development of a more global agenda.

In this Article, to address these gaps, we systematically investigated combined predictors of social cognition in older individuals through a multicentric computational approach (Fig. 1a). We sought to determine whether the traditional effects of age (Fig. 1b) and patient–control differences (Fig. 1c) are indeed the primary drivers of performance variability in social cognition tasks. We assembled 1,063 participants (>50 years) from nine countries to maximize sample diversity. Our outcomes of interest were facial emotion recognition, mentalizing and a social cognition total score (that is, the combination of both measures) using a well-characterized battery, the mini-social cognition and emotional assessment (mini-SEA)[33]. In the mini-SEA, participants are asked to identify the emotion depicted in a subset of photos from the Ekman series and to identify unintended transgression of social rules (that is, faux pas) in short stories. The potential predictors of social cognition comprised the following factors: (1) clinical diagnosis (HCs, SCC, MCI, Alzheimer's disease (AD) and behavioral variant frontotemporal dementia (bvFTD)); (2) demographics (sex (female or male), age (years), education (years) and country income as a proxy of socioeconomic status (HICs and UMICs)[34]); (3) cognition (cognitive[35–37] and executive function[38,39] screening scores); (4) brain reserve (gray matter volume derived from voxel-based morphometry (VBM) analysis[40] and functional connectivity strength derived from seed analysis[41] of the resting-state functional magnetic resonance imaging (fMRI) networks: salience network (SN)[42], default mode network (DMN)[43], executive network (EN)[44], visual network (VN)[45] and motor network (MN[46])); and (5) in-scanner motion artifacts (average translation and rotation parameters during the resting-state sequence). The analysis consisted of three distinct model sets. The initial set focused on behavioral data, spanning clinical diagnosis, demographics and cognition. The second set integrated structural brain reserve factors (gray matter volume) with the previous behavioral predictors. Lastly, the third set incorporated functional connectivity metrics and motion artifacts, building upon the predictors from both the first and second sets.

We anticipate that healthy individuals, female[13,14], younger in age[13–15], highly educated[13,15,16], from HICs[17], with better cognitive and executive abilities[16,19] and with higher brain reserve[20] will exhibit higher emotion recognition, mentalizing and total scores. However, traditional factors (that is, age and diagnosis) influencing social cognition as reported in homogeneous and stereotypical samples are hypothesized to show a reduced predictive value[21]. Our findings have the potential to advance our understanding of social cognition in aging populations by elucidating the factors that contribute to performance variability in current assessments. This knowledge can inform the development of tailored predictive models and tools to assess and improve social cognition in brain health and age-related diseases.

Results

Traditional effects (age and diagnosis) on social cognition

Simple linear regression analyses showed that advanced age significantly predicted worse emotion recognition, mentalizing and the social cognition total score (Fig. 1b and Extended Data Table 1). Linear mixed-effects models[47] controlling for sex, age, education and country of origin revealed that the diagnosis had a significant effect on emotion recognition ($F = 32.88$, $P < 0.0001$ and $\eta_p^2 = 0.12$), mentalizing ($F = 59.72$, $P < 0.0001$ and $\eta_p^2 = 0.2$) and the total score ($F = 63.93$, $P < 0.0001$ and $\eta_p^2 = 0.21$). Šidák-corrected post hoc tests showed that HC and SCC groups outperformed MCI, AD and bvFTD groups in the three measures, and that individuals with bvFTD performed significantly worse than those with AD in emotion recognition (Fig. 1c). No other significant between-group differences were found. Diagnosis effects on mentalizing ($F = 12.75$, $P < 0.0001$ and $\eta_p^2 = 0.17$) and the total score ($F = 14.36$, $P < 0.0001$ and $\eta_p^2 = 0.08$) were maintained when including the participants' performance in the mentalizing control questions of the test[33] as a covariate of no interest (Extended Data Fig. 1). This analysis confirms that results were not entirely explained by a lack of attention to or understanding of the stimuli.

Combined predictors of social cognition

Support vector regression (SVR) models[48] were used to predict social cognition (emotion recognition, mentalizing and the total score) from the complete set of potential predictors. Multicollinearity between predictors is assumed and addressed in our models (Methods). In any case, as multicollinearity concerns the relationships among predictors[49], it does not inherently imply any circular relationship with the outcomes of our models (that is, social cognition). Data were harmonized across countries (using equivalence tables[50], scale transformation and *z*-scores estimation), and 170 missing values were imputed using a sklearn iterative imputer with Bayesian ridge regression[51]. SVR models were optimized using Bayesian optimization[52] with $k = 3$ cross-validation for tuning the hyperparameters on training (70%) and testing (30%) folds, with ten repetitions. Feature selection was performed using backward elimination[53] to identify each model's top predictors (in order of relevance). To obtain the final models, 1,000 optimized SVR regressors were trained and tested for each outcome variable using a bootstrap approach, setting aside median-stratified 30% of the data as a test partition. We report the average models' performance and largest false discovery rate-corrected *P* values (statsmodels version 0.13.2) on the test partition of the data. Analyses were performed in the full sample ($n = 998$, after removing participants with invalid scores) and in subsamples with neuroimaging recordings, including structural MRI ($n = 598$) and resting-state fMRI ($n = 388$) sequences.

Behavioral predictors

The first set of models assessed whether behavioral data (clinical diagnosis, demographics and cognition) were able to predict social cognition (Fig. 2a). The model using emotion recognition as the outcome variable was significant ($R^2 = 0.35$, confidence interval (CI) (95%) 0.07, $f^2 = 0.53$, $F = 22.31$ and $P < 0.0001$). The best predictors of emotion recognition were, in order of importance, cognition ($\beta = 29.67$ and $P < 0.0001$), executive function ($\beta = 18.98$ and $P < 0.0001$), education ($\beta = 7.88$ and $P < 0.0001$), sex ($\beta = 7.11$ and $P < 0.0001$), country income ($\beta = 5.95$ and $P < 0.0001$) and diagnosis ($\beta = 5.51$ and $P < 0.0001$).

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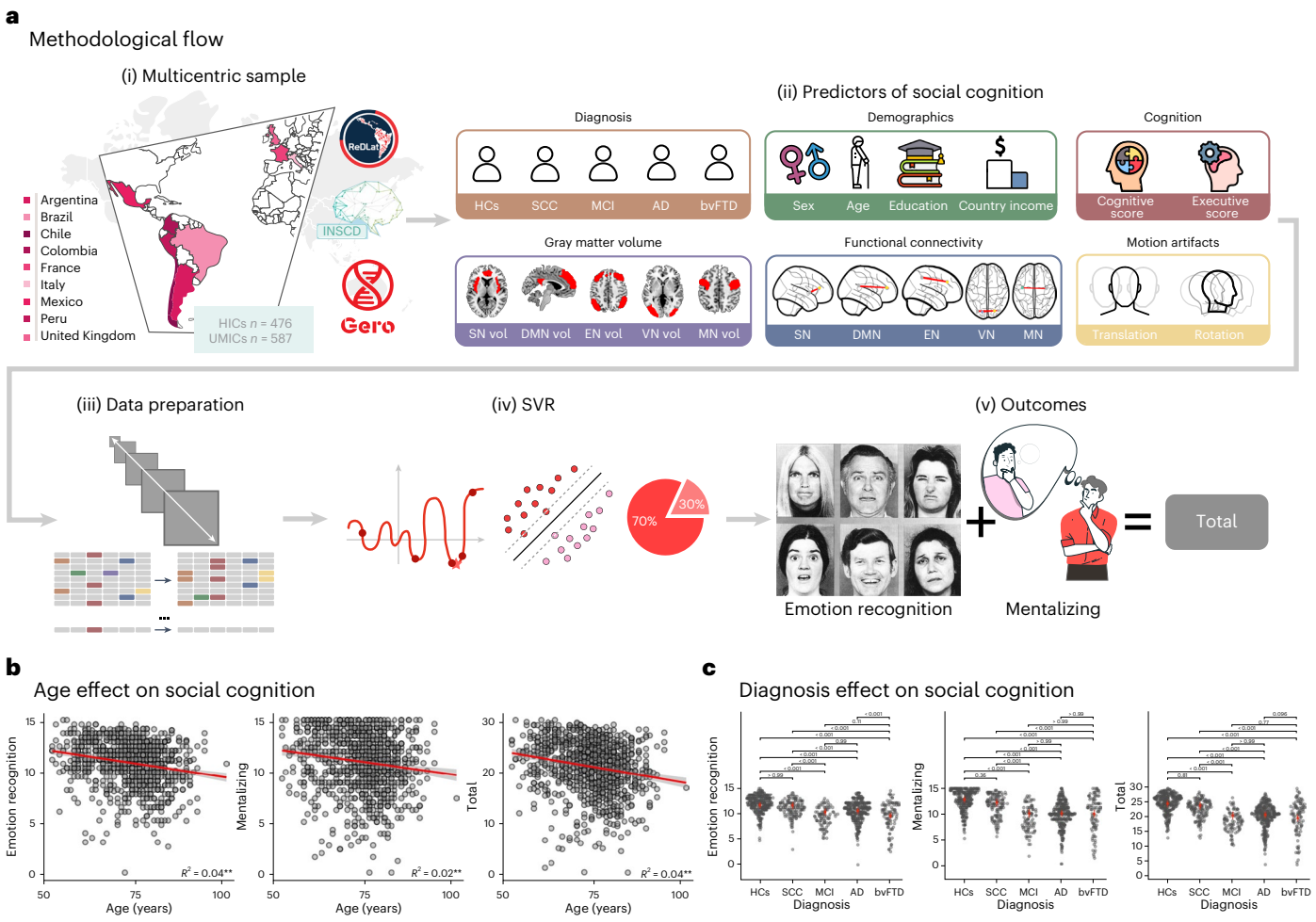

Fig. 1 | Analysis pipeline and traditional effects of age and diagnosis on social cognition performance. a, (i) Participants were recruited from HICs (Chile, France, Italy and the United Kingdom) and UMICs (Argentina, Brazil, Colombia, Peru and Mexico) through ReDLat, the INSCD and GERO. (ii) Diagnosis, demographics, cognition, gray matter volume (vol) and fMRI resting-state functional connectivity of brain networks, and in-scanner motion artifacts were entered into computational models as predictors of social cognition. (iii) Data were harmonized across countries (including scale transformation) and missing values were imputed. (iv) The analysis involved Bayesian optimization with $k = 3$ cross-validation for tuning the hyperparameters in 70:30 train and test partitioning and SVR models using a bootstrap approach. (v) Outcome variables were facial emotion recognition, mentalizing and a social cognition total score from the mini-SEA battery. Emotion recognition image was reproduced from ref. 118. **b**, Age significantly predicted worse performance in emotion recognition, mentalizing and the total score across the full sample ($n = 998$). Data were analyzed with simple linear regression analysis. Red lines and gray shadings represent the best-fit line for each simple linear regression with 95% confidence bands. $^{**}P < 0.0001$ (for details, see Extended Data Table 1). **c**, Participants with MCI ($n = 96$), AD ($n = 339$) and bvFTD ($n = 102$) performed significantly worse in social cognition relative to HCs ($n = 316$) and the SCC group ($n = 145$), and participants with bvFTD also performed significantly worse than those with AD in emotion recognition. Data were analyzed with linear mixed-effects models[47] controlling for sex, age, education and country of origin. The red dots and lines display the mean and s.d. *P* values are corrected for multiple comparisons using the Šidák method.

Age was not a significant contributor for emotion recognition ($\beta = 3.53$ and $P = 0.97$). Mentalizing was significantly predicted ($R^2 = 0.34$, CI (95%) 0.09, $f^2 = 0.52$, $F = 21.76$ and $P < 0.0001$) by cognition ($\beta = 45.31$ and $P < 0.0001$), executive function ($\beta = 29.87$ and $P < 0.0001$), education ($\beta = 16.23$ and $P < 0.0001$), diagnosis ($\beta = 7.17$ and $P < 0.0001$) and country income ($\beta = 7$ and $P < 0.0001$). Sex and age were not significant ($\beta = 2.51$, $P = 0.85$ and $\beta = 2.34$, $P = 0.84$, respectively). Finally, the social cognition total score was successfully predicted ($R^2 = 0.44$, CI (95%) 0.06, $f^2 = 0.79$, $F = 33.07$ and $P < 0.0001$) by cognition ($\beta = 63.13$ and $P < 0.0001$), executive function ($\beta = 41.13$ and $P < 0.0001$), education ($\beta = 23.23$ and $P < 0.0001$), diagnosis ($\beta = 11.50$ and $P < 0.0001$) and sex ($\beta = 8.05$ and $P < 0.0001$). Country income and age were not significant ($\beta = 6.55$, $P = 0.12$ and $\beta = 3.75$, $P = 0.79$, respectively). The results were similar when assessed without data imputation (Extended Data Table 2), and in the subsamples with structural MRI (Extended Data Table 3) or resting-state fMRI (Extended Data Table 4) recordings. A consistent pattern of behavioral predictors was also found when stratifying the sample by sex (Extended Data Table 5) and analyzing HCs separately (Extended Data Table 6). Taken together, better cognitive and executive functions and higher educational level consistently emerged as the top predictors of social cognition performance, above diagnosis and other demographic characteristics.

Behavioral and structural brain reserve predictors

The second set of models included the previous behavioral predictors plus one level of brain reserve (gray matter volume) as predictors of social cognition performance (Fig. 2b). The model predicting emotion recognition was significant ($R^2 = 0.28$, CI (95%) 0.09, $f^2 = 0.39$, $F = 5.45$ and $P < 0.0001$) and included the following features: cognition ($\beta = 27.25$ and $P < 0.0001$), executive function ($\beta = 20.37$ and $P < 0.0001$), SN volume ($\beta = 20.19$, $T = 116.11$ and $P < 0.0001$), EN volume ($\beta = 15.44$ and $P < 0.0001$), sex ($\beta = 9.79$ and $P < 0.0001$), MN volume ($\beta = 9.01$

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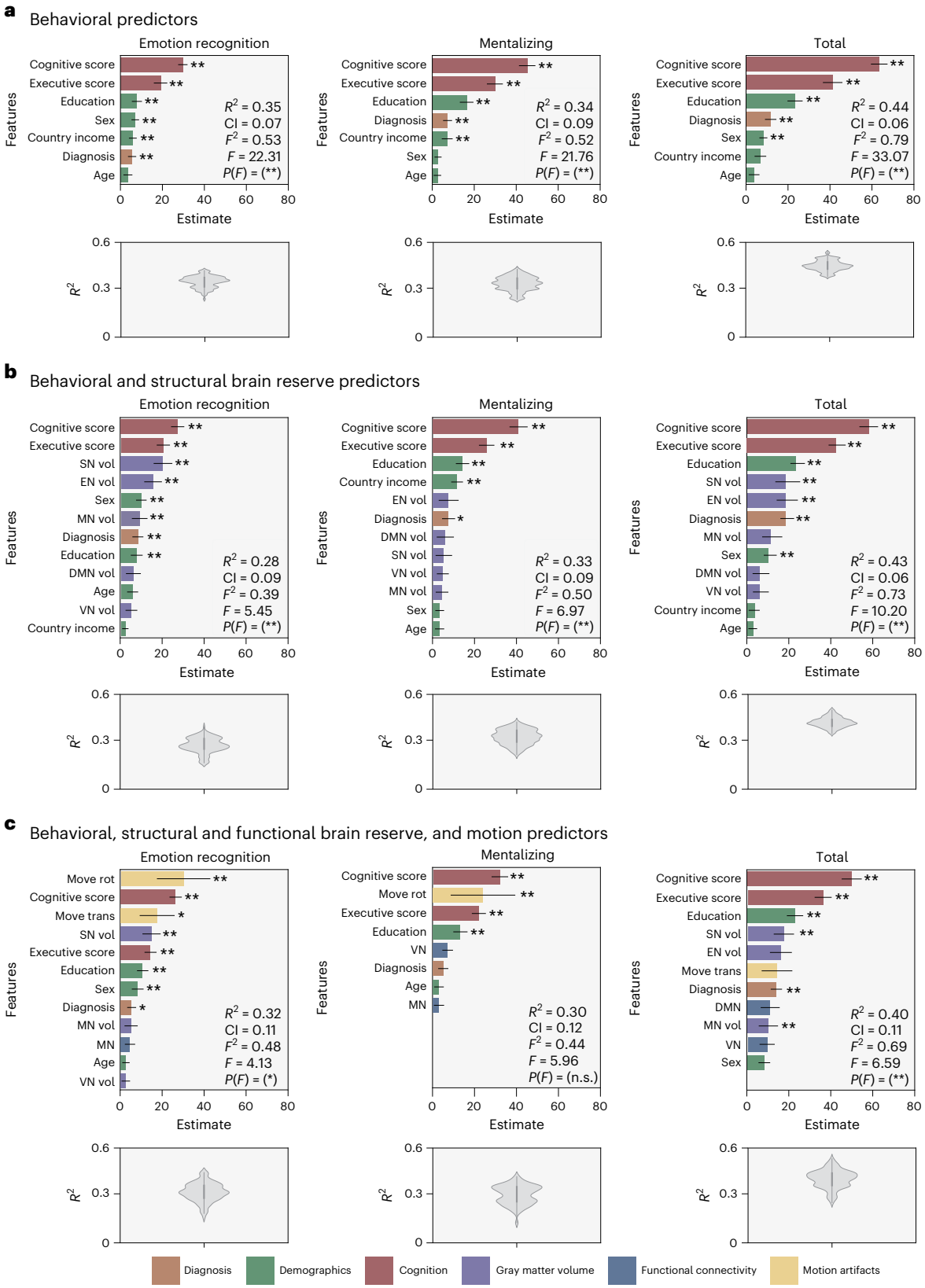

Fig. 2 | SVR results. a, Models including diagnosis, demographics and cognition as predictors of social cognition performance (n = 998). **b**, Models including one level of brain reserve (gray matter volume) together with behavioral features as predictors of social cognition performance (n = 598). **c**, Models including resting-state functional connectivity features (brain networks and motion artifacts) as predictors of social cognition performance in addition to behavioral and gray matter volume predictors (n = 388). Bars plots represent the β coefficient and CI associated with each predictor in each model. Violin plots show the distribution of R^2 values in the test partitions of the data from the bootstrap approach (n = 1,000 optimized SVR models). Thick lines inside density plots display the IQR and whiskers show maximum and minimum values of R^2. The translucid panel displays a nonsignificant model. Move rot: rotation movements; move trans: translation movements. *P < 0.05 and **P < 0.01 (details are provided in the main text).

and $P < 0.0001$), diagnosis ($\beta = 8.14$ and $P < 0.0001$) and education ($\beta = 7.58$ and $P < 0.0001$). DMN volume ($\beta = 5.99$ and $P = 0.92$), age ($\beta = 5.63$ and $P = 0.23$), VN volume ($\beta = 5.04$ and $P = 0.69$) and country income ($\beta = 2.12$ and $P = 0.77$) were not significant. Mentalizing was also successfully predicted ($R^2 = 0.33$, CI (95%) 0.09, $f^2 = 0.5$, $F = 6.97$ and $P < 0.0001$) by cognition ($\beta = 40.82$ and $P < 0.0001$), executive function ($\beta = 25.60$ and $P < 0.0001$), education ($\beta = 14.10$ and $P < 0.0001$), country income ($\beta = 11.49$ and $P < 0.0001$) and diagnosis ($\beta = 7.43$ and $P = 0.02$). EN volume ($\beta = 7.48$ and $P = 0.6$), DMN volume ($\beta = 5.87$ and $P = 0.83$), SN volume ($\beta = 5.18$ and $P = 0.78$), VN volume ($\beta = 4.46$ and $P = 0.95$), MN volume ($\beta = 4.31$ and $P = 0.44$), sex ($\beta = 3.20$ and $P = 0.82$) and age ($\beta = 3.15$ and $P = 0.22$) were not significant. The social cognition total score was significantly predicted ($R^2 = 0.43$, CI (95%) 0.06, $f^2 = 0.73$, $F = 10.2$ and $P < 0.0001$) by cognition ($\beta = 57.93$ and $P < 0.0001$), executive function ($\beta = 42.49$ and $P < 0.0001$), education ($\beta = 23.21$ and $P < 0.0001$), SN volume ($\beta = 18.38$ and $P < 0.0001$), EN volume ($\beta = 18.13$ and $P < 0.0001$), diagnosis ($\beta = 18.12$ and $P < 0.0001$) and sex ($\beta = 10.13$ and $P < 0.0001$). MN volume ($\beta = 11.11$ and $P = 0.89$), DMN volume ($\beta = 5.95$ and $P = 0.73$), VN volume ($\beta = 5.88$ and $P = 0.95$), country income ($\beta = 3.58$ and $P = 0.82$) and age ($\beta = 2.88$ and $P = 0.72$) were not significant. Models including only gray matter predictors were not significant (Extended Data Table 7). Overall, higher cognitive and executive functions and years of education remained among the top predictors of social cognition (together with diagnosis). The higher the gray matter volume of SN, EN and MN hubs, the larger the contributions to emotion recognition.

Behavioral and structural–functional brain predictors

The last set of models included the previous two set of predictors (behavior and gray matter volume) plus functional connectivity and motion artifact predictors (Fig. 2c). Emotion recognition was significantly ($R^2 = 0.32$, CI (95%) 0.11, $f^2 = 0.48$, $F = 4.13$ and $P < 0.01$) predicted by rotation movements ($\beta = 30.07$ and $P < 0.0001$), cognition ($\beta = 26.24$ and $P < 0.0001$), translation movements ($\beta = 17.40$ and $P < 0.03$), SN volume ($\beta = 14.72$, $P < 0.034$ and $P < 0.0001$), executive function ($\beta = 14.24$ and $P < 0.0001$), education ($\beta = 10.49$ and $P < 0.0001$), sex ($\beta = 8.10$ and $P < 0.001$) and diagnosis ($\beta = 5.22$ and $P < 0.036$). MN volume ($\beta = 4.95$ and $P = 0.46$), MN ($\beta = 4.42$ and $P = 0.28$), age ($\beta = 2.48$ and $P = 0.96$) and VN volume ($\beta = 2.41$ and $P = 0.93$) were not significant. Mentalizing was not successfully predicted in this model ($R^2 = 0.3$, CI (95%) 0.11, $f^2 = 0.44$, $F = 5.96$ and $P = 1$). Finally, the social cognition total score was significantly ($R^2 = 0.4$, CI (95%) 0.11, $f^2 = 0.69$, $F = 6.59$ and $P < 0.0001$) predicted and characterized by cognition ($\beta = 49.85$ and $P < 0.0001$), executive function ($\beta = 36.16$ and $P < 0.0001$), education ($\beta = 22.67$ and $P < 0.0001$), SN volume ($\beta = 17.32$ and $P < 0.0001$), diagnosis ($\beta = 13.73$ and $P < 0.0001$) and MN volume ($\beta = 9.90$ and $P = 0.003$). EN volume ($\beta = 15.90$ and $P = 0.23$), translation movements ($\beta = 14.02$ and $P = 0.83$), DMN ($\beta = 10.76$ and $P = 0.6$), VN ($\beta = 9.31$ and $P = 0.15$) and sex ($\beta = 7.95$ and $P = 0.7$) did not contribute to the model. Models including functional connectivity and motion features alone (Extended Data Table 8) and functional connectivity and motion features together with gray matter predictors (that is, only brain reserve, Extended Data Table 9) were not significant. Briefly, better cognitive and executive functions, higher education and more gray matter volume of SN hubs remained among the best predictors of social cognition together with diagnosis. While brain networks did not make significant contributions to the models, higher motion artifacts were associated with social cognition.

Discussion

We investigated the top predictors of social cognition in aging. Two main strengths enabled us to address this issue systematically: (1) the use of a diverse sample comprising 1,063 older individuals from nine countries, representing a wide range of demographics and socioeconomic contexts, and (2) the development of a multicentric computational approach that thoroughly examined the combined influence of various contributing factors. The results from SVR showed that combinations of behavioral, brain reserve (gray matter volume) and motion artifact features explained between 28% and 44% of the variance in tasks involving emotion recognition and mentalizing, with large effect sizes ($f^2 = 0.39–0.79$). Higher cognitive and executive functions consistently predicted higher social cognition across models. More years of education was also ranked among the top predictors of social cognition in most models. Such factors had a larger influence than age across models, a finding that persisted even within the group of HCs. Furthermore, a direct comparison between nested regression models unveiled that, according to different statistical criteria (R^2, adjusted R^2, likelihood ratio test, Akaike information criterion, Bayesian information criterion and root mean squared error), the model encompassing all potential predictors surpassed the model with age (Supplementary Information and Supplementary Table 1). Moreover, while diagnostic differences in social cognition followed the expected pattern, with MCI and dementia groups performing poorer than HCs and SCC groups[9,54], and bvFTD underperforming AD only in emotion recognition[55], diagnosis was not the primary determinant of performance variability. Across models, the diagnosis effect was overshadowed by other factors, particularly cognition, executive functions and education. Finally, structural (to a lesser extent) and functional brain reserve measures had small and partial effects in the models' performance. These results challenge traditional interpretations of age-related decline, patient–control differences and brain associations of social cognition, emphasizing the importance of heterogeneous factors. This knowledge has implications for developing tailored predictive social cognition models in diverse aging populations. It also informs the development of more robust assessment and intervention tools, ultimately improving brain health and quality of life.

The strong influence of cognitive and executive functions on social cognition performance is consistent with a growing body of evidence suggesting that age-related decline in a wide range of paradigms is dependent on task demands[16,17,19,56–58]. Accurately identifying the emotions of others partially rests on attention allocation, and attentional disturbances can lead to misrecognition of emotions and the development of affective symptoms[59]. Mentalizing relies on the capacity to inhibit one's own perspective in favor of adopting that of others, a process that requires executive functions (that is, working memory and set shifting)[19]. Thus, the well-established decrease on these general-purpose abilities in older adults[60] may explain social cognition decline. Relatedly, as in previous studies[16,61], higher education also consistently emerged among the top predictors of social cognition performance. Taken together, cognition and education might represent proxies of the cognitive reserve in aging, namely the ability to cope with brain pathology to maintain function[62]. While a previous work showed that cognitive reserve was not associated with social cognition in older adults[63], such evidence came from a homogeneous HIC population, potentially failing to capture the diversity of individual differences.

Another factor that predicted better emotion recognition and mentalizing was country income (HICs). The World Bank country classification[34] represents a national level measure of the socioeconomic background of an individual (that is, social and monetary wealth or power)[64]. Socioeconomic status is known to have robust effects in predicting brain health outcomes in older individuals[65] and dementia[23]. However, its impact on social cognition and emotional processing has only recently been addressed, pointing to a mediator role of cognitive and executive functions[17]. Our results expand this emergent research by revealing a unique contribution of socioeconomic status to social cognition performance. Finally, female sex was associated with improved emotion recognition (but not mentalizing), as previously observed[13,63]. Women's advantage in identifying others' emotions may be a result of gender-role stereotypes[66]. However, more research is needed to determine the underlying mechanisms of such advantage. In summary, our behavioral models suggested that, in addition to cognition,

executive functions, and education, socioeconomic status and sex play an important role in some social cognition domains.

Including brain reserve measures (gray matter volume) in the model architecture did not explain the additional variance in social cognition performance. Moreover, the model that solely utilized gray matter features did not yield predictive value. Cognitive and executive abilities remained the top predictors of emotion recognition, mentalizing and the total score. Consequently, cognitive reserve may be more relevant than structural brain reserve for social cognition outcomes, potentially reflecting the deployment of active mechanisms (for example, processing resources or compensation) that facilitate coping with pathology beyond brain size[62]. Following cognitive factors, higher gray matter volume of the main hubs of the SN (bilateral insula and anterior cingulate cortex[42]), the EN (bilateral middle frontal and inferior parietal cortex[67]) and the MN (precentral cortex[67]) was associated with better emotion recognition. This finding is consistent with the role of these regions in detecting and attending to salient stimuli[68], as well as in the embodied processing of emotions through mirroring mechanisms[69,70]. Conversely, gray matter volume did not significantly contribute to mentalizing. A possible explanation for this discrepancy could be the higher cognitive demands necessary to mental state inference as opposed to facial emotion recognition, resulting in cognition capturing more variance.

The last set of models showed that fMRI brain network connectivity failed to predict social cognition when combined with behavioral features and brain volume (and also when considered independently). Moreover, mentalizing was not significantly predicted in these analyses. In contrast, translation and rotation in-scanner motion artifacts were associated with better emotion recognition (together with cognition, executive functions, SN volume, education, sex and diagnosis). Considering the existing evidence on resting-state functional connectivity associations with social cognition (particularly the SN[68] and the DMN[43,71]), this pattern of results may appear unusual. However, it is becoming increasingly evident that clinical and demographic heterogeneity can hinder the identification of brain–behavior associations[26,72]. Predictive models from homogeneous samples fail to characterize nonstereotypical individuals, particularly from multisite cohorts[72], with in-scanner motion parameters representing a major source of model failure[26]. In brief, brain networks failed to explain social cognition performance, with cognitive and motion features emerging as top predictors in the emotion model, emphasizing the need to consider disparate sources of variability in future studies.

This work reveals that social cognition components in aging are shaped by heterogeneous factors, adding to recent literature on the demographic, socioeconomic and sociocultural determinants of social cognition[12–14,18,23]. Contrary to mainstream research, our results indicate that age and clinical diagnosis are not the primary drivers of individual differences in social cognition across diverse settings. Although both factors showed the expected effects when assessed independently, such influences attenuate or vanish when other factors are considered. Previous works have failed to detect age associations with social cognition after accounting for cognitive[57,58] and mood (that is, depression[58]) factors. Older adults might even show improved mentalizing abilities when considering education, race and ethnicity in explanatory models[12]. Thus, age-related normal and pathological brain mechanisms may become less influential when accounting for sample diversity.

These unforeseen findings extend beyond the social cognition field. Most studies on factors associated with brain health and pathological aging have been performed in HICs[73]. However, risk may differ in underrepresented regions such as Latin America where multiple social and health disadvantages converge, including poverty, limited access to formal education and healthcare, and barriers to a healthy lifestyle[21–23,74]. Indeed, recent evidence from Latin American older adults underscores a more pronounced influence of heterogeneous and disparity-related factors (that is, social determinants of health, education, mental health symptoms and physical activity) on healthy aging relative to the age and sex traditional factors[21]. The present work aligns with this research and contributes to current calls of increasing sample diversity[26,30,72], aiming to make cognitive and behavioral science more situated[75,76].

These findings also question whether social cognition can be distinguished from broader cognitive function. Existing answers in the literature are inconclusive[3,77]. As cognitive and executive functions mediate social cognition[16,17,19,56–58], there are important considerations. First, even after accounting for those factors, older adults might still experience sociocognitive difficulties[4,78]. Second, while socioeconomic disadvantages harm cognitive and executive functions, they can paradoxically enhance social cognition in some settings[18]. Third, cognition and social cognition engage partially distinct neural correlates[79] and are linked to somewhat different functional outcomes[80,81]. Our results point to a partial overlap between domains. While social cognition showed a strong association with cognition in the regression models, the expected differences in performance between patients and controls on the mini-SEA persisted after covarying for the mentalizing control questions of the task. This suggests that patients' performance might not be entirely attributed to a failure in processing task stimuli (that is, lack of attention or understanding). However, as control of task performance does not fully capture complex cognitive/executive processes, further research is needed in older adults.

This work carries relevant implications. Our results inform the development of tailored predictive models that acknowledge the diverse characteristics of the population under study. This may lead to more accurate and ethical interpretations[82], improving decision-making in region-specific approaches to brain health. The results suggest a more nuanced approach to social cognition assessment by reducing cognitive demands, accounting for potential attentional or comprehension issues (for example, by analyzing control stimuli)[77], and developing norms adjusted for years of education and country. These recommendations are particularly relevant in light of recent calls to use standardized social cognition tasks in clinical settings to support patient characterization and differential diagnosis[2,11,83]. In the realm of interventions, the findings emphasize the need for contextual approaches when addressing social cognition impairments[84,85]. Demographic, socioeconomic and cognitive diversity might modulate the response to social cognition interventions and their impact on everyday function. Tailored predictive models, more sensitive assessments, heterogeneity-robust methods and situated interventions in social cognition may prove crucial to advance brain health equity.

Some limitations and additional lines of research must be acknowledged. First, although we used one of the most widely used social cognition assessment[13,33,54], it has low ecological validity. Future studies should incorporate more naturalistic stimuli[86]. Also, other social cognition components (such as empathy and compassion[87]) should be investigated in older adults. Second, we included only a limited number of countries with unbalanced participants, reducing the possibilities for cross-country interpretations. Two clinical groups (SCC and MCI) were enrolled exclusively in one country and recruitment center, potentially introducing confounds. However, separate analyses of this cohort (Supplementary Table 2) and the remaining groups collectively (Supplementary Table 3) yielded results consistent with our main findings. Relatedly, assembling participants from multiple sites and using different cognitive and scanning protocols may introduce disparate sources of uncontrolled variability. However, our methods, combining data harmonization (equivalence tables for cognitive data[50], site-specific *z*-scores for fMRI data[54,88–92] and missing data imputation[51]) and machine learning algorithms (involving stratified data partition, hyperparameter tuning, cross-validation, SVR[48] with Ridge regularization[51], backward feature selection[53] and generalization to unseen samples) prove robust to handle unbalanced and diverse samples[21,50], multicollinearity between predictors[49] and the identification of top

contributing factors[93]. Taken together, our approach is suitable to leverage the intrinsic heterogeneity of our multi-setting sample. In any case, global approaches to brain health need larger and more balanced samples to perform more systematic comparisons across regions. Third, we used a country-level index of socioeconomic status, potentially lacking accuracy in reflecting the precise circumstances of each participant, particularly in Latin America, which is known by its marked inequality. Other socioeconomic indicators such as the Gini index or the human capital index might prove more sensitive to better capture the distinct inequalities inherent to each region. Moreover, global socioeconomic status indexes should be complemented with measures at the individual or family level (for example, household income and occupation prestige). Fourth, the cross-sectional nature of our study impedes causal conclusions. Further research should adopt longitudinal designs to understand the temporal dynamics between disparate factors and social cognition performance in brain health and disease. Finally, given the small sample size of our clinical groups and the disbalance across countries and sites, our design was unsuitable for exploring diagnosis stratification. Studies involving larger and balanced clinical cohorts should examine whether social cognition relies on distinct factors across different patient groups. Available evidence emphasizes a primary deficit in bvFTD and a secondary impairment in AD that would depend on memory and other cognitive functions[83,94]. This approach could be enriched by a more diverse range of social cognition predictors (for example, ethnicity and genetics) and diagnostic categories (for example, language variants of FTD[95] and other neurodegenerative and neuropsychiatric disorders[96]).

Conclusions

Using a multicentric computational approach across three levels of analysis, our findings reveal that social cognition in aging is shaped by a heterogeneous array of cognitive and sociodemographic factors. The most influential predictors were cognitive and executive functions (together with education in most models), which outweighed the impact of age, clinical diagnosis and brain reserve. The results challenge traditional interpretations of age decline, patient–control differences and brain associations of social cognition. We emphasize the need to consider heterogeneous factors in further studies, with implications for predictive models, assessments and interventions, aimed at developing more global and inclusive approaches to brain health.

Methods

Participants

The study comprised 1,063 participants aged between 50 and 98 years (mean age 71.56 years, s.d. 8.42 years, 64.6% women, mean years of education 12.01, s.d. years of education 5). The recruitment was performed across 13 sites in 9 countries, 4 HICs (Chile, France, Italy and the United Kingdom, $n = 476$) and 5 UMICs (Argentina, Brazil, Colombia, Peru and Mexico, $n = 587$) as classified according to the World Bank[34]. The sample included HCs and individuals with different conditions associated with aging (SCC, MCI, AD and bvFTD, see below). Participants were recruited from different international consortia, including the Multi-Partner Consortium to Expand Dementia Research in Latin America (ReDLat)[97], the International Network on Social Condition Disorders (INSCD)[13] and the Geroscience Center for Brain Health and Metabolism (GERO)[98].

All participants underwent extensive neurological, neuropsychological and neuropsychiatric examinations comprising semistructured interviews, standardized cognitive assessments and MRI scanning (when available). Clinical diagnoses were performed by multidisciplinary expert teams following established criteria as detailed below. The diagnostic process did not include the mini-SEA, ruling out a potential selection bias. HCs ($n = 325$) had preserved cognition and no history of neurological or psychiatric conditions. Participants with SCC ($n = 145$) presented cognitive complaints either self-reported or reported by a knowledgeable informant, scored 0.5 or less on the Clinical Dementia Rating scale[99] and had preserved functional abilities[98]. The MCI group ($n = 96$) was composed of participants fulfilling the same criteria as those with SCC but scoring <22 in the Montreal Cognitive Assessment (MoCA)[36], the most frequently used cut-off to detect MCI[100]. Individuals with AD ($n = 389$) fulfilled the National Institute of Neurological and Communicative Disorders and Stroke–AD and Related Disorders Association criteria[101], were in early and middle stages of the disease, presented memory deficits and were functionally impaired. Individuals with bvFTD ($n = 114$) fulfilled the revised Rascovsky criteria[102], were in the early and middle stages of the disease, exhibited prominent behavioral changes, lacked primary language deficits and had functional impairment. Supporting the clinical diagnosis of neurodegenerative conditions, an analysis of a subsample of participants with available structural MRI data revealed temporal and frontoparietal atrophy in the AD group[101], and fronto-temporo-insular atrophy in the bvFTD group[103] (Supplementary Fig. 1 and Supplementary Table 4). Demographic and cognitive information of each participant group is provided in Supplementary Table 5. The institutional review board of each recruitment site and the executive committee of the ReDLat consortium approved this study. All participants signed informed consent as approved by their respective center's ethics committee. No compensation was provided for this study.

Social cognition assessment

Participants completed the mini-SEA, a short battery designed to assess two social cognition domains: facial emotion recognition and mentalizing[33]. In the facial emotion recognition subtest, participants are asked to identify the emotion being depicted by an individual in 35 different photos from the Ekman series. The following options are provided: fear, sadness, disgust, anger, happiness, surprise and neutral. Each correct item is given one point. The mentalizing subtest consists of an adaptation of the Faux Pas test. Participants are presented with ten short stories and asked to identify if the protagonist committed an unintended transgression of a social rule (that is, a faux pas). Each story also includes two control questions to assess general understanding. The maximum score for this subtest is 40 points. The scores of emotion recognition and mentalizing subtests are converted to a score of 15 each and then summed, resulting in a total score of 30, with higher scores representing better performance. From the full sample, 6.11% of participants ($n = 65$) were removed for lacking a valid score either in the emotion recognition or the mentalizing subtest, resulting in a final sample of 998 individuals.

Predictors of social cognition

The set of potential predictors of social cognition included:

(a) Behavioral features

(a.1) Diagnosis, HCs, SCC, MCI, AD and bvFTD.

(a.2) Demographics, sex (female, male), age (years), education (years) and country income (HICs and UMICs) following the World Bank classification[34].

(a.3) Cognition

(a.3.1) Cognitive score, derived from harmonized scores in the Addenbrooke's Cognitive Examination III (ref. 37), the Mini-Mental State Examination (MMSE)[35] and the MoCA[36]. For details about these tools, see Supplementary Information and Supplementary Table 5 for the number of participants assessed with each tool in each group and the 'Data harmonization' section.

(a.3.2) Executive score, derived from harmonized scores in the INECO Frontal Screening (IFS)[39] and the Frontal Assessment Battery (FAB)[38] (Supplementary Information, Supplementary Table 5 and 'Data harmonization').

(b) Brain reserve features

(b.1) Gray matter volume, average volume of key hubs of the SN, the DMN, the EN, the MN and the VN from the Automated Anatomical Labeling atlas[104] calculated using VBM analysis (see below).

(b.2) Functional connectivity, average connectivity strength of the SN, the DMN, the EN, the VN and the MN calculated via seed analysis of the fMRI resting-state series (see below).

(c) Motion artifacts, average translation and rotation movements estimated during the preprocessing of the fMRI sequence.

Neuroimage acquisition and preprocessing

This section is reported following recommendations from the Organization for Human Brain Mapping[105]. Whole-brain structural three-dimensional T1-weighted and resting-state sequences were obtained for 598 (195 HCs, 91 SCC, 53 MCI, 194 AD and 65 bvFTD) and 388 (125 HCs, 91 SCC, 52 MCI, 82 AD and 38 bvFTD) participants, respectively, across acquisition centers. For the resting-state sequence, participants were instructed to remain still, awake, with eyes closed and not to think about anything in particular. Demographic and cognitive information of these subsamples are provided in Supplementary Tables 6 and 7. The scanning protocols followed by each center are detailed in Supplementary Tables 8 and 9. Structural MRI scans were preprocessed using the DARTEL Toolbox following standard procedures for VBM[40] through the Statistical Parametric Mapping software (SPM12 (ref. 106)). Functional images were preprocessed using the Data Processing Assistant for Resting-State fMRI toolbox (v.4.4 (ref. 107)) following published procedures[41] (details in Supplementary Information). Six movement parameters (right, forward, up, pitch, roll and yaw) were estimated during realignment to calculate average translation and rotation movements per participant (group statistics are reported in Supplementary Table 10).

Data harmonization

Two procedures were applied to increase the number of participants with homogeneous cognitive and executive measures and harmonize the available data. First, cognitive screening measures were harmonized using equivalence tables following recommended methods[50,108,109], validated for multicentric studies using data from Latin American underrepresented samples[50]. This procedure allows for MoCA and ACE scores to be estimated using MMSE scores and the MMSE scores using MoCA and ACE scores. As a result, a total of three new converted–harmonized variables were added. Then, the MMSE and MoCA scores were transformed from a 0–30 to a 0–100 scale and averaged with the ACE score to create a single cognitive score per participant (scale 0–100). All participants had a cognitive score. Finally, IFS and FAB scores were also transformed into a 0–100 scale and averaged to obtain a single executive score per participant. Both the IFS and the FAB have previously shown significant associations with classical executive tests across healthy individuals and patients with dementia, as well as adequate discriminatory accuracy to differentiate between those groups[110]. This suggests these measures have similar external validity. A correlational analysis using the subsample of participants with both tests revealed a strong correlation between the IFS and FAB transformed scores (Pearson's $r = 0.72$ and $P < 0.0001$). This result further supports comparability (inferential equivalence[111]) between such measures. In total, 833 participants had an executive score. Second, we calculated z-scores for demographic (sex, age, education and country income), cognitive (cognitive score and executive score), gray matter, functional connectivity and motion artifacts variables. For neuroimaging variables, z-scores were estimated using normative data from each fMRI acquisition site according to the following equation:

$$x_z = \frac{x - \mu}{s}$$

where x_z is the new value, x is the original raw score, μ is the mean score for HCs from the center to which the participant belongs and s is the standard deviation for HCs from the site or center to which the participant belongs.

Using site-specific z-scores is a standard procedure for harmonizing neuroimaging data in multicentric studies on neurodegeneration[54,88–92]. This procedure directly compares different sites and imaging modalities[112], controlling for protocol effects (for example, various magnetic fields and scanner-related artifacts) while addressing potential neuroanatomical/neurofunctional differences between normative groups[92]. Site-specific standardization proves more robust than conventional covariance methods in controlling for protocol effects without losing information on diagnosis effects[92].

Data imputation

A sklearn iterative imputer with Bayesian ridge regression[51] (Python 3.7) was used to impute missing values for age ($n = 4$), education ($n = 2$) and executive score ($n = 165$). This algorithm applies a multivariate imputing strategy, modeling a column with missing values as a function of other features and using the estimate for imputation. Each feature is imputed sequentially allowing the usage of prior imputed values on the model that predicts later features. This process is repeated several times, allowing increasingly better estimates of missing values to be calculated as the missing values for each feature are estimated.

SVR models

To generate predictions of continuous variables (emotion recognition, mentalizing and total scores) from multimodal features (behavior, brain reserve and motion artifacts), we ran SVR models using the sklearn[51] package in Python 3.7. SVR is a variation of support vector machine that allows linear and nonlinear regression. SVR transforms the feature space to establish a hyperplane that best fits the training data, while also minimizing the generalization error on new, unseen data[48]. The hyperplane is defined as the set of all points x in the feature space such that:

$$\mathbf{w} \cdot x + b = 0$$

where $\mathbf{w}$ is the weight vector, b is the bias term and $\cdot$ denotes the dot product.

The SVR model seeks to find the weight vector $\mathbf{w}$ and bias term b that satisfy this constraint, while also minimizing the distance between the hyperplane and the training data. The distance is measured using a loss function, typically the ε-insensitive loss:

$$L(y, \hat{y}) = \max(|y - \hat{y}| - \varepsilon, 0)$$

where y is the true target value, $\hat{y}$ is the predicted target value and ε is a small constant that defines the width of the margin around the hyperplane. The loss function penalizes errors that exceed ε, but ignores errors that fall within ε.

To find the optimal weight vector $\mathbf{w}$ and bias term b, SVR introduces two slack variables ξ_i and $\hat{\xi}_i$ for each training example, which allow for violations of the margin and the ε-insensitive loss, respectively. The optimization problem for SVR is then given by:

Minimize:

$$\frac{1}{2}||\mathbf{w}||^2 + C\left(\sum_{i=1}^{n}(\xi_i + \hat{\xi}_i)\right)$$

Subject to:

$$y_i - \langle \mathbf{w}, \phi(x_i) \rangle \leq \varepsilon + \xi_i \quad i = 1, \cdots, n$$

$$\langle \mathbf{w}, \phi(x_i) \rangle - y_i \leq \varepsilon + \hat{\xi}_i \quad i = 1, \cdots, n$$

$$\xi_i \geq 0, \ \hat{\xi}_i \geq 0 \quad i = 1, \cdots, n$$

where C is a hyperparameter that controls the trade-off between the margin width and the number of violations allowed, and n is the number of training examples. The first term in the objective function

encourages a wide margin, while the second term penalizes violations of the margin and the ε-insensitive loss.

SVR can be extended to handle nonlinear regression tasks by using a kernel function to map the input data to a higher-dimensional feature space, where the problem may become linearly separable. The optimization problem then becomes:

Minimize:

$$-\frac{1}{2}\sum_{i,j=1}^{n}(\alpha_i-\hat{\alpha}_i)(\alpha_i-\hat{\alpha}_i)K(x_i,x_j)-\varepsilon$$

Subject to:

$$\sum_{i=1}^{n}(\alpha_i-\hat{\alpha}_i)=0$$

$$0\le\alpha_i,\hat{\alpha}_i\le C$$

where $K(x_i, x_j)$ is the kernel function that computes the inner product between the mapped feature vectors, and α_i and are Lagrange multipliers that determine the importance of each training example in defining the hyperplane. The kernel function allows SVR to learn complex, nonlinear relationships between the input features and the target variable.

Sklearn's SVR uses the L2 regularization term (Ridge regularization) in its function[51]. This regularization term helps control the model's complexity, prevents overfitting[113], and mitigates the impact of multicollinearity by penalizing the magnitudes of regression coefficients[49]. The strength of the L2 regularization is controlled by the *C* hyperparameter, where a smaller value of *C* corresponds to a stronger regularization effect.

Hyperparameter tuning

A Bayesian optimization[52] with $k = 3$ cross-validation was applied for tuning the hyperparameters. A radial basis function kernel was used with optimized gamma value. Models with the best hyperparameters were trained on a training sample (70%) and tested in a testing set (30%), with ten repetitions (Supplementary Information).

Feature selection

We used a backward elimination approach[53] to select the most significant predictors for each model. For each iteration, we dropped the predictor with the largest *P* value until we reached a statistically significant model, a predictor with a *P* value that became statistically significant or a model with two predictors. This procedure allowed us to automatically rank predictors based on their contribution to the model's prediction accuracy without assuming a priori theoretical importance, which is required when classical statistical methods are applied[93]. Moreover, backward elimination mitigates the impact of multicollinearity between predictors by removing correlated features[49].

Statistical analyses

VBM analysis. Using VBM preprocessed structural images, we calculated the average gray matter volume (ml, corrected by total intracranial volume) of 116 regions of the Automated Anatomical Labeling atlas[104] to create gray matter volume indexes of the main hubs of the SN (average of the bilateral anterior cingulum and insula volume[42]), the DMN (average of the bilateral medial frontal and posterior cingulate volume[43]), the EN (average of the bilateral middle frontal and inferior parietal volume[67]), the VN (average of the bilateral occipital volume[67]) and the MN (average of the bilateral precentral volume[67]).

Functional connectivity analysis. The functional connectivity strength of the SN, the DMN, the EN, the VN and the MN was calculated using seed analysis. Two bilateral seeds were placed on cubic regions of interest (voxel size 7 × 7 × 7) for each network: the dorsal anterior cingulate cortex for the SN[42], MNI coordinates 10, 34, 24 and −10, 34, 24; the posterior cingulate cortex for the DMN[43], MNI coordinates 3, −54, 27 and −3, −54, 27; the middle frontal gyri for the EN[44], MNI coordinates 30, −2, 62 and −30, −2, 62; the primary visual cortex for the VN[45], MNI coordinates 8, −92, 8 and −8, −92, 8; and the primary motor cortex for the MN[46], MNI coordinates 32, −30, 68 and −32, −30, 68. The Pearson correlation coefficient between the averaged blood-oxygen-level-dependent signal of each pair of seeds and voxels comprised in standard masks[114] typically involved in each resting-state network was used to extract one feature per network for each participant. The statistical significance of the resting-state networks was tested by comparing them with null surrogate models. This approach enables robust statistical evaluations to ensure that the results observed are not obtained by chance but represent a true characteristic of the underlying system[115]. The surrogate data technique is based on comparing a particular property of the data (a discriminating statistic) with the distribution of the same property calculated in a set of constructed signals (surrogates) that match the original dataset but do not possess the property that is being tested. To this end, we used Fourier transform-based surrogates to recreate the brain's complex-system dynamics, including uncorrelated and correlated noise, coupling between different brain areas, and synchronization. We found that all the computed resting-state networks were statistically significant against null connectivity (SN: $P = 0.02$; DMN: $P = 0.02$; EN: $P = 0.03$; VN: $P = 0.02$ and MN: $P = 0.03$), further corroborating our connectivity methods.

Age effects on social cognition. Simple linear regression analyses were used to evaluate the predictive value of age on emotion recognition, mentalizing and the social cognition total score. Analyses were performed in R software (version 4.1.3). The alpha threshold was set at $P < 0.05$. Effect size was evaluated with f^2, following Cohen's criteria,[116] stating that 0.02 indicates a small effect, 0.15 indicates a medium effect and 0.35 indicates a large effect.

Social cognition performance across diagnostic groups. Linear mixed-effects models[47] were performed in R (version 4.1.3) to examine diagnosis effects and between-group differences in emotion recognition, mentalizing and the total score. Sex, age and education were entered in the model as covariates of no interest, and the participant's country of origin was entered as a random effect. Additional analyses included the participants' performance in the mentalizing control questions of the mini-SEA as a covariate of no interest. Post hoc tests were corrected using the Šidák method. The alpha threshold was set at $P < 0.05$. Effect size was evaluated with η_p^2 where 0.01 indicates a small effect, 0.06 indicates a medium effect and 0.14 indicates a large effect[117].

SVR model estimation and performance assessment. We trained and tested 1,000 optimized SVR models for each outcome variable to obtain the final models using a bootstrap approach. We applied *P* value correction for false discovery rate using statsmodels (version 0.13.2) and set aside a median-stratified 30% of the data as a test set. To evaluate the models' performance, we used four statistics: the coefficient of determination R^2, 95% CI, Cohen's f^2 (ref. 116), Fisher's *F* test and the largest corrected *P* values. Outlier results (R^2 < interquartile range (IQR) − 1.5 × s.d. and R^2 > IQR + 1.5 × s.d.) were discarded to improve average estimates.

Inclusion and ethics statement

This work involved a collaboration between scientists in multiple countries including Argentina, Brazil, Chile, Colombia, France, Italy, Ireland, Mexico, Peru and the United Kingdom. All contributors have been listed as co-authors in acknowledgement to their work. Researchers from Latin America have led the study conceptualization, data analysis and manuscript writing. Collaborators established and agreed

on their respective roles and responsibilities before the research began. Each site that participated in this study has retained ownership of all materials shared for research purposes.

All methods were performed in accordance with relevant guidelines and regulations provided by the Declaration of Helsinki. The institutional review board of each recruitment site and the executive committee of the ReDLat consortium approved this study. All participants signed an informed consent as approved by their respective center's ethics committee. No compensation was provided for this study.

Reporting summary

Further information on research design is available in the Nature Portfolio Reporting Summary linked to this article.

Data availability

Anonymized data that support results of this study are publicly available on the Open Science Framework and GitHub (https://github.com/AI-BrainLat-team/Global-Mini-SEA). Preprocessed MRI/fMRI data are available on the Open Science Framework (https://osf.io/s754k/).

Code availability

Code used in this study is available for download on the Open Science Framework (https://osf.io/s754k/) and GitHub (https://github.com/AI-BrainLat-team/Global-Mini-SEA).

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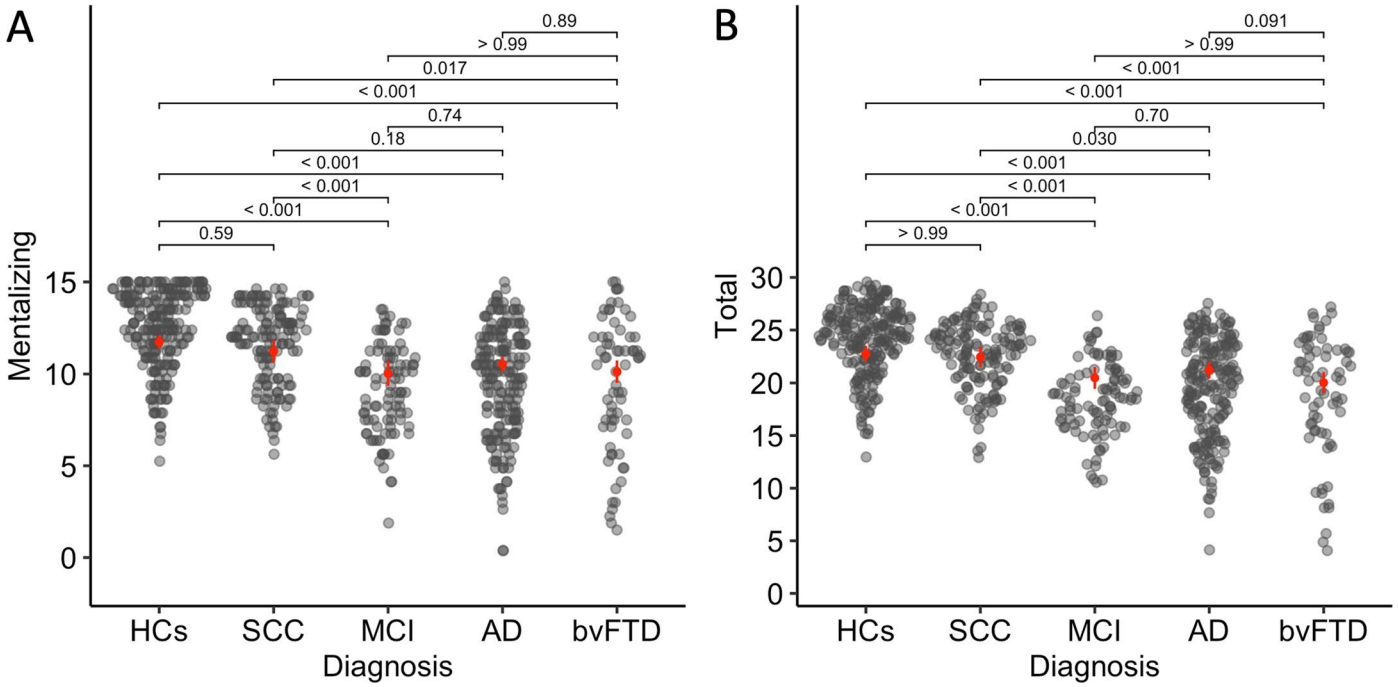

Extended Data Fig. 1 | Diagnosis effect on social cognition when covarying for mentalizing control questions. (A) MCI, AD, and bvFTD participants showed significantly worse mentalizing than HCs. Participants with MCI and bvFTD also showed poorer performance in mentalizing than those with SCC. No other significant between-group differences were found. (B) Participants with MCI (n = 96), AD (n = 202), and bvFTD (n = 68) had poorer overall performance in social cognition than HCs (n = 229) and participants with SCC (n = 145). No other significant between-group differences were found. Data were analyzed using linear mixed-effects models controlling for sex, age, education, country of origin, and performance in the mentalizing control questions of the test using the subsample of 740 participants for whom such scores were available. The red dots and lines display the mean and SD. P values are corrected for multiple comparisons using the Sidak method. AD: Alzheimer's disease, bvFTD: behavioral variant frontotemporal dementia, HCs: healthy controls, MCI: mild cognitive impairment, SCC: subjective cognitive complaints.

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Extended Data Table 1 | Simple regression results including age as isolated predictor of social cognition

Outcome	Predictor	Estimate	Model stats
Emotion recognition	Age	-0.05	R^2 = 0.04 f^2 = 0.05 F = 47.49 P = 9.792e-12
Mentalizing	Age	-0.05	R^2 = 0.02 f^2 = 0.02 F = 22.22 P = 2.78e-06
Total	Age	-0.1	R^2 = 0.04 f^2 = 0.04 F = 42 P = 1.435e-10

Data were analyzed with simple linear regression analysis. N=998.

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Extended Data Table 2 | Models with behavioral predictors in the sample without data imputation

Outcome	Features	Estimate	P value	Model stats
Emotion recognition	Cognitive score	27.91	< 0.0001	R^2 = 0.36 CI (95%) = 0.08 f^2 = 0.57 F = 19.68 P < 0.0001
	Executive score	14.64	< 0.0001	
	Education	7.53	< 0.0001	
	Sex	7.18	< 0.0001	
	Diagnosis	6.96	< 0.0001	
	Country income	4.42	0.5	
	Age	2.57	0.83	
Mentalizing	Cognitive score	37.25	< 0.0001	R^2 = 0.32 CI (95%) = 0.08 f^2 = 0.47 F = 16.16 P < 0.0001
	Executive score	20.72	< 0.0001	
	Education	11.57	< 0.0001	
	Diagnosis	5.88	0.52	
	Country income	4.42	0.59	
	Age	2.93	0.96	
	Sex	1.66	0.97	
Total	Cognitive score	56.53	< 0.0001	R^2 = 0.42 CI (95%) = 0.07 f^2 = 0.75 F = 26.14 < 0.0001
	Executive score	31.01	< 0.0001	
	Education	18.21	< 0.0001	
	Diagnosis	12.43	< 0.0001	
	Sex	6.78	< 0.001	
	Age	4.49	0.56	
	Country income	3.14	0.62	

Data were analyzed using support vector regression (SVR) models with Bayesian optimization for hyperparameter tuning and backward elimination for feature selection. For each outcome, we report the largest false discovery rate-corrected P value from 1000 bootstrapped SVR models. Results are shown on the test partition of the data. N = 827.

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Extended Data Table 3 | Models with behavioral predictors in the subsample with structural MRI data

Outcome	Features	Estimate	P value	Model stats
Emotion recognition	Cognitive score	21.49	< 0.0001	R^2 = 0.32 CI (95%) = 0.08 f^2 = 0.48 F = 11.70 P < 0.0001
	Executive score	16.40	< 0.0001	
	Education	7.71	< 0.0001	
	Diagnosis	7.65	< 0.0001	
	Sex	5.59	< 0.0001	
	Age	2.48	0.88	
	Country income	1.84	0.94	
Mentalizing	Cognitive score	27.73	< 0.0001	R^2 = 0.33 CI (95%) = 0.10 f^2 = 0.50 F = 12.21 P < 0.0001
	Executive score	17.85	< 0.0001	
	Education	15.18	< 0.0001	
	Diagnosis	8.44	< 0.0001	
	Country income	6.19	< 0.0001	
	Age	3.60	0.99	
	Sex	1.67	0.98	
Total	Cognitive score	41.13	< 0.0001	R^2 = 0.42 CI (95%) = 0.07 f^2 = 0.74 F = 18.10 P < 0.0001
	Executive score	30.31	< 0.0001	
	Education	21.05	< 0.0001	
	Diagnosis	15.76	< 0.0001	
	Sex	5.06	0.95	
	Age	2.88	0.95	
	Country income	2.52	0.81	

Data were analyzed using support vector regression (SVR) models with Bayesian optimization for hyperparameter tuning and backward elimination for feature selection. For each outcome, we report the largest false discovery rate-corrected P value from 1000 bootstrapped SVR models. Results are shown on the test partition of the data. N=598.

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Extended Data Table 4 | Models with behavioral predictors in the subsample with resting-state fMRI data

Outcome	Features	Estimate	P value	Model stats
Emotion recognition	Cognitive score	19.21	< 0.0001	R^2 = 0.32 CI (95%) = 0.11 f^2 = 0.47 F = 7.33 P < 0.0001
	Executive score	11.08	< 0.0001	
	Diagnosis	6.22	< 0.0001	
	Education	5.83	< 0.0001	
	Sex	4.34	0.59	
	Country income	2.96	0.86	
	Age	2.09	0.93	
Mentalizing	Cognitive score	27.30	< 0.0001	R^2 = 0.32 CI (95%) = 0.10 f^2 = 0.49 F = 7.56 P < 0.0001
	Executive score	16.56	< 0.0001	
	Education	13.15	< 0.0001	
	Country income	7.43	0.001	
	Diagnosis	5.31	< 0.0001	
	Age	3.12	0.71	
	Sex	2.19	0.94	
Total	Cognitive score	38.15	< 0.0001	R^2 = 0.43 CI (95%) = 0.10 f^2 = 0.77 F = 11.95 P < 0.0001
	Executive score	25.54	< 0.0001	
	Education	19.70	< 0.0001	
	Diagnosis	12.29	< 0.0001	
	Sex	5.92	0.13	
	Age	3.50	0.93	
	Country income	3.10	0.83	

Data were analyzed using support vector regression (SVR) models with Bayesian optimization for hyperparameter tuning and backward elimination for feature selection. For each outcome, we report the largest false discovery rate-corrected P value from 1000 bootstrapped SVR models. Results are shown on the test partition of the data. N=388.

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Extended Data Table 5 | Models with behavioral predictors in each sex separately

Group	Outcome	Features	Estimate	P value	Model stats
Women (N = 644)	Emotion recognition	Cognitive score	31.3	< 0.0001	R^2 = 0.34 CI (95%) = 0.08 f^2 = 0.52 F = 16.26 P < 0.0001
		Executive score	18.74	< 0.0001	
		Education	11.73	< 0.0001	
		Diagnosis	5.94	< 0.0001	
		Country income	2.4	0.81	
		Age	1.76	0.99	
	Mentalizing	Cognitive score	36.49	< 0.0001	R^2 = 0.37 CI (95%) = 0.09 f^2 = 0.6 F = 18.85 P < 0.0001
		Executive score	26.86	< 0.0001	
		Education	14.4	< 0.0001	
		Country income	6.55	0.02	
		Diagnosis	6.15	< 0.0001	
		Age	4.57	0.58	
	Total	Cognitive score	56.12	< 0.0001	R^2 = 0.46 CI (95%) = 0.06 f^2 = 0.87 F = 27.41 P < 0.0001
		Executive score	37.29	< 0.0001	
		Education	22.07	< 0.0001	
		Diagnosis	10.74	< 0.0001	
		Country income	4.67	0.49	
		Age	3.04	0.77	
Men (N = 354)	Emotion recognition	Executive score	14.72	< 0.0001	R^2 = 0.28 CI (95%) = 0.09 f^2 = 0.41 F = 6.9 P < 0.0001
		Cognitive score	13.33	< 0.0001	
		Country income	4.38	0.003	
		Education	4.35	0.03	
		Diagnosis	3.41	0.52	
		Age	2.14	0.99	
	Mentalizing	Cognitive score	23.18	< 0.0001	R^2 = 0.22 CI (95%) = 0.11 f^2 = 0.3 F = 5.01 P < 0.0001
		Executive score	15.58	< 0.0001	
		Education	8.59	0.006	
		Age	6.48	< 0.001	
		Diagnosis	5.74	0.21	
		Country income	3.16	0.81	
	Total	Cognitive score	29.33	< 0.0001	R^2 = 0.33 CI (95%) = 0.1 f^2 = 0.51 F = 8.62 P < 0.0001
		Executive score	27.77	< 0.0001	
		Education	15.88	< 0.0001	
		Diagnosis	9.64	< 0.0001	
		Age	7.77	0.1	
		Country income	3.67	0.99	

Data were analyzed using support vector regression (SVR) models with Bayesian optimization for hyperparameter tuning and backward elimination for feature selection. For each outcome, P values were corrected for false discovery rate from 1000 bootstrapped SVR models and aggregated using the Fisher method for combining independent P values. Results are shown on the test partition of the data.

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Extended Data Table 6 | Models with behavioral predictors in healthy controls

Outcome	Features	Estimate	P value	Model stats
Emotion recognition	Cognitive score	4.41	< 0.0001	R^2 = 0.09 CI (95%) = 0.09 f^2 = 0.09 F = 1.28 P < 0.0001
	Sex	4.23	0.001	
	Executive score	3.8	0.35	
	Age	3.34	0.24	
	Education	1.8	0.95	
	Country income	1.22	0.89	
Mentalizing	Education	5.4	< 0.001	R^2 = 0.08 CI (95%) = 0.11 f^2 = 0.08 F = 1.24 P < 0.0001
	Cognitive score	4.56	0.52	
	Executive score	3.93	0.97	
	Age	2.73	0.43	
	Country income	1.89	0.97	
	Sex	1.28	0.89	
Total	Executive score	8.56	< 0.0001	R^2 = 0.15 CI (95%) = 0.1 f^2 = 0.18 F = 2.61 P < 0.0001
	Cognitive score	7.79	< 0.0001	
	Education	7.75	< 0.0001	
	Age	6.18	0.57	
	Sex	2.28	0.85	
	Country income	1.68	0.99	

Data were analyzed using support vector regression (SVR) models with Bayesian optimization for hyperparameter tuning and backward elimination for feature selection. For each outcome, P values were corrected for false discovery rate from 1000 bootstrapped SVR models and aggregated using the Fisher method for combining independent P values. Results are shown on the test partition of the data. N=316.

https://doi.org/10.1038/s44220-023-00164-3

Extended Data Table 7 | Models with grey matter predictors

Outcome	Features	Estimate	P value	Model stats
Emotion recognition	SN vol	16.05	< 0.0001	R^2 = 0.008 CI (95%) = 0.07 f^2 = 0.01 F = 0.35 P = 1
	EN vol	15.31	< 0.0001	
	MN vol	12.24	< 0.0001	
	VN vol	8.27	0.16	
	DMN vol	7.98	0.03	
Mentalizing	SN vol	6.16	0.82	R^2 = -0.02 CI (95%) = 0.07 f^2 = -0.02 F = -0.7 P = 1
	DMN vol	6.14	0.88	
	VN vol	5.99	0.65	
	MN vol	4.44	0.96	
	EN vol	4.35	0.98	
Total	SN vol	14.18	0.001	R^2 = 0.01 CI (95%) = 0.07 f^2 = 0.01 F = 0.5 P = 1
	MN vol	12.21	0.003	
	EN vol	11.57	0.62	
	VN vol	9.97	0.59	
	DMN vol	9.34	0.55	

Data were analyzed using support vector regression (SVR) models with Bayesian optimization for hyperparameter tuning and backward elimination for feature selection. For each outcome, we report the largest false discovery rate-corrected P value from 1000 bootstrapped SVR models. Results are shown on the test partition of the data. DMN: default mode network, EN: executive network, MN: motor network, SN: salience network, VN: visual network, vol: volume. N=598.

https://doi.org/10.1038/s44220-023-00164-3

Extended Data Table 8 | Models with functional connectivity and motion artifacts predictors

Outcome	Features	Estimate	P value	Model stats
Emotion recognition	Move rot	29.42	< 0.0001	R^2 = 0.03 CI (95%) = 0.09 f^2 = 0.03 F = 1.27 P = 1
	Move trans	16.35	< 0.001	
	DMN	5.19	0.02	
Mentalizing	Move trans	12.79	< 0.0001	R^2 = -0.005 CI (95%) = 0.07 f^2 = -0.004 F = -0.17 P = 1
	Move rot	23.92	< 0.0001	
	DMN	8.03	< 0.0001	
Total	DMN	19.84	< 0.0001	R^2 = -0.03 CI (95%) = 0.07 f^2 = -0.03 F = -0.45 P = 1
	EN	7.84	0.004	
	SN	16.61	< 0.0001	

Data were analyzed using support vector regression (SVR) models with Bayesian optimization for hyperparameter tuning and backward elimination for feature selection. For each outcome, we report the largest false discovery rate-corrected P value from 1000 bootstrapped SVR models. Results are shown on the test partition of the data. DMN: default mode network, EN: executive network, move rot: rotation movements, move trans: translation movements, SN: salience network. N=388.

https://doi.org/10.1038/s44220-023-00164-3

Extended Data Table 9 | Models with grey matter, functional connectivity, and motion artifacts predictors

Outcome	Features	Estimate	P value	Model stats
Emotion recognition	Move rot	26.24	0.35	R^2 = 0.02 CI (95%) = 0.1 f^2 = 0.02 F = 0.24 P = 1
	Move trans	16.30	0.46	
	SN vol	15.02	< 0.0001	
	EN vol	12.74	< 0.0001	
	DMN vol	11.29	< 0.0001	
	DMN	7.41	0.68	
	MN vol	7.33	0.87	
	VN vol	5.99	0.96	
	MN	5.09	0.48	
	EN	3.92	0.71	
	VN	3.87	0.63	
	SN	3.30	0.43	
Mentalizing	Move rot	21.87	0.84	R^2 = -0.01 CI (95%) = 0.08 f^2 = -0.01 F = -0.09 P = 1
	DMN vol	16.58	< 0.0001	
	Move trans	11.94	0.79	
	VN vol	10.31	< 0.0001	
	DMN	9.59	< 0.0001	
	VN	8.95	0.26	
	EN vol	8.34	0.47	
	MN vol	7.88	0.94	
	SN vol	6.93	0.74	
	SN	6.5	0.7	
	MN	3.99	0.69	
	EN	2.5	0.87	
Total	Move rot	22.98	0.71	R^2 = 0.01 CI (95%) = 0.07 f^2 = 0.01 F = 0.16 P = 1
	DMN vol	19.58	< 0.0001	
	SN vol	17.56	< 0.0001	
	EN vol	15.68	< 0.0001	
	Move trans	15.16	0.91	
	DMN	15.13	< 0.0001	
	VN vol	14.45	< 0.001	
	SN	12.97	< 0.0001	
	VN	11.26	0.03	
	MN vol	9.76	0.25	
	EN	4.48	0.83	
	MN	3.02	0.96	

Data were analyzed using support vector regression (SVR) models with Bayesian optimization for hyperparameter tuning and backward elimination for feature selection. For each outcome, we report the largest false discovery rate-corrected P value from 1000 bootstrapped SVR models. Results are shown on the test partition of the data. DMN: default mode network, EN: executive network, MN: motor network, move rot: rotation movements, move trans: translation movements, SN: salience network, VN: visual network, vol: volume. N=388.

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Reporting Summary

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Statistics

For all statistical analyses, confirm that the following items are present in the figure legend, table legend, main text, or Methods section.

n/a	Confirmed
☐	☒ The exact sample size (*n*) for each experimental group/condition, given as a discrete number and unit of measurement
☐	☒ A statement on whether measurements were taken from distinct samples or whether the same sample was measured repeatedly
☐	☒ The statistical test(s) used AND whether they are one- or two-sided *Only common tests should be described solely by name; describe more complex techniques in the Methods section.*
☐	☒ A description of all covariates tested
☐	☒ A description of any assumptions or corrections, such as tests of normality and adjustment for multiple comparisons
☐	☒ A full description of the statistical parameters including central tendency (e.g. means) or other basic estimates (e.g. regression coefficient) AND variation (e.g. standard deviation) or associated estimates of uncertainty (e.g. confidence intervals)
☐	☒ For null hypothesis testing, the test statistic (e.g. *F*, *t*, *r*) with confidence intervals, effect sizes, degrees of freedom and *P* value noted *Give P values as exact values whenever suitable.*
☒	☐ For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings
☒	☐ For hierarchical and complex designs, identification of the appropriate level for tests and full reporting of outcomes
☐	☒ Estimates of effect sizes (e.g. Cohen's *d*, Pearson's *r*), indicating how they were calculated

Our web collection on statistics for biologists contains articles on many of the points above.

Software and code

Policy information about availability of computer code

Data collection	No specific software was used for data collection.
Data analysis	Descriptive statistics, regression analyses, model comparisons, and linear mixed effects models were performed in R software version 4.3.1. Structural images were analyzed using the Statistical Parametric Mapping software version 12 (SPM12). Functional images were analyzed using the Data Processing Assistant for Resting-State fMRI toolbox (DPARSF v.4.4) which works calling the SPM12 and the Resting-State fMRI Data Analysis Toolkit (REST v.1.7). Support vector regression analyses were performed in Python 3.7 using sklearn package and statsmodels (version 0.13.2). Code is available for download on the Open Science Framework (https://osf.io/s754k/) and GitHub (https://github.com/AI-BrainLat-team/Global-Mini-SEA).

For manuscripts utilizing custom algorithms or software that are central to the research but not yet described in published literature, software must be made available to editors and reviewers. We strongly encourage code deposition in a community repository (e.g. GitHub). See the Nature Portfolio guidelines for submitting code & software for further information.

Data

Policy information about availability of data

All manuscripts must include a data availability statement. This statement should provide the following information, where applicable:

- Accession codes, unique identifiers, or web links for publicly available datasets
- A description of any restrictions on data availability
- For clinical datasets or third party data, please ensure that the statement adheres to our policy

Anonymized data that support results of this study are publicly available on the Open Science Framework (https://osf.io/s754k/) and GitHub (https://github.com/AI-BrainLat-team/Global-Mini-SEA). Preprocessed MRI/fMRI data are available on the Open Science Framework (https://osf.io/s754k/).

Research involving human participants, their data, or biological material

Policy information about studies with human participants or human data. See also policy information about sex, gender (identity/presentation), and sexual orientation and race, ethnicity and racism.

Reporting on sex and gender	We use the term sex to allude to a biological attribute, determined through self-report. Data on gender was not collected. Sex was included in all analysis as a potential explanatory variable.
Reporting on race, ethnicity, or other socially relevant groupings	We do not include data on race or ethnicity. Country income was used as a proxy of socioeconomic status (high-income countries, upper-middle-income countries) as defined by the World Bank.
Population characteristics	The study comprised 1063 participants between 50 and 98 years (mean age = 71.56, SD age = 8.42, 64.6% women, mean years of education = 12.01, SD years of education = 5). The recruitment was performed across 13 sites in 9 countries, 4 high-income countries (Chile, France, Italy, United Kingdom, n = 476) and 5 upper-middle-income countries (Argentina, Brazil, Colombia, Peru, Mexico, n = 587) as classified according to the World Bank. The sample included healthy controls and individuals with different conditions associated with aging (subjective cognitive complaints, mild cognitive impairment, Alzheimer's disease, and behavioral variant frontotemporal dementia). Non-representative convenience and community-dwelling samples were recruited from different international consortia (see below).
Recruitment	Participants were recruited from international consortia: the Multi-Partner Consortium to Expand Dementia Research in Latin America (ReDLat), the International Network on Social Condition Disorders (INSCD), and the Geroscience Center for Brain Health and Metabolism (GERO).
Ethics oversight	The IRB of each recruitment site and the Executive Committee of the ReDLat consortium approved this study. All participants signed informed consent as approved by their respective center's ethics committee. No compensation was provided for this study.

Note that full information on the approval of the study protocol must also be provided in the manuscript.

Field-specific reporting

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☐ Life sciences ☒ Behavioural & social sciences ☐ Ecological, evolutionary & environmental sciences

For a reference copy of the document with all sections, see nature.com/documents/nr-reporting-summary-flat.pdf

Behavioural & social sciences study design

All studies must disclose on these points even when the disclosure is negative.

Study description	This is an observational, cross-sectional, quantitative study. We systematically investigated combined predictors of social cognition in older individuals through a multicentric computational approach. We assembled 1063 participants (> 50 years) from 9 countries to maximize sample diversity. Our outcomes of interest were facial emotion recognition, mentalizing, and a social cognition total score (i.e., the combination of both measures) using a well-characterized battery, the Mini-Social Cognition and Emotional Assessment (Mini-SEA). The potential predictors of social cognition comprised the following factors: (a) clinical diagnosis (healthy controls, subjective cognitive complains, mild cognitive impairment, Alzheimer's disease, and behavioral variant frontotemporal dementia); (b) demographics [sex (female, male), age (years), education (years), and country income as a proxy of socioeconomic status (high-income countries, upper-middle-income countries)]; (c) cognition (cognitive and executive function screening scores); (d) brain reserve (grey matter volume derived from voxel-based morphometry analysis and functional connectivity strength derived from seed analysis of the resting-state fMRI networks: salience network, default mode network, executive network, visual network, and motor network); and (e) in-scanner motion artifacts (average translation and rotation parameters during the resting-state sequence). The analysis consisted of three distinct model sets. The initial set focused on behavioral data, spanning clinical diagnosis, demographics, and cognition. The second set integrated structural brain reserve factors (grey matter volume) with the previously mentioned behavioral predictors. Lastly, the third set incorporated functional connectivity metrics and motion artifacts, building upon the

	predictors from both the first and second sets. Data were analyzed using support vector regression models with train/test partition, Bayesian optimization and cross validation for hyperparameter tuning, and backward elimination for feature selection.
Research sample	The study comprised 1063 participants between 50 and 98 years (mean age = 71.56, SD age = 8.42, 64.6% women, mean years of education = 12.01, SD years of education = 5). The recruitment was performed across 13 sites in 9 countries, 4 high-income countries (Chile, France, Italy, United Kingdom, n = 476) and 5 upper-middle-income countries (Argentina, Brazil, Colombia, Peru, Mexico, n = 587) as classified according to the World Bank. The sample included healthy controls and individuals with different conditions associated with aging (subjective cognitive complaints, mild cognitive impairment, Alzheimer's disease, and behavioral variant frontotemporal dementia). Non-representative convenience and community-dwelling samples were recruited from different international consortia: the Multi-Partner Consortium to Expand Dementia Research in Latin America (ReDLat), the International Network on Social Condition Disorders (INSCD), and the Geroscience Center for Brain Health and Metabolism (GERO). ReDLat is a project aimed to combine genomic, neuroimaging, and behavioral (clinical, cognitive, socioeconomic) data to improve dementia characterization in diverse populations across centers in Latin America and the US. INSCD is a network created for the study of social cognition in brain diseases which reunites different centers across the world. GERO is a longitudinal study in Chile aimed to characterize multimodal determinants of aging in the region. The IRB of each recruitment site and the Executive Committee of the ReDLat consortium approved this study. All participants signed informed consent as approved by their respective center's ethics committee. No compensation was provided for this study.
Sampling strategy	We used non-representative convenience samples from ReDLat and INSCD. We used a community-dwelling sample (Santiago, Chile) from GERO. Our sample size is considered adequate for standalone machine learning models.
Data collection	All participants underwent extensive neurological, neuropsychological, and neuropsychiatric examinations comprising semistructured interviews, standardized cognitive assessments, and MRI scanning (when available). Clinical diagnoses were performed by multidisciplinary expert teams following established criteria. Outcome data (MiniSEA social cognition battery) were collected using a computer by trained examiners blind to the study hypotheses (no other person was present). MRI data were collected using 1.5 or 3 tesla scanners by trained professionals.
Timing	We used existing datasets collected at different time points (ReDLat: 01/2014-06/2022, INSCD: 01/2010-06/2022, GERO: 01/2017-06/2022)
Data exclusions	From the full sample (n = 1063), 6.11% of participants (n = 65) were removed for lacking a valid score either in the emotion recognition or the mentalizing subtest, resulting in a final sample of 998 individuals.
Non-participation	We use preexisting datasets from ReDLat, INSCD, and GERO. No new participants were collected for this study.
Randomization	This is an observational, cross-sectional, quantitative study designed to examine combined predictors of social cognition across the sample. No experimental manipulations were performed. Therefore, randomization was not applicable.

Reporting for specific materials, systems and methods

We require information from authors about some types of materials, experimental systems and methods used in many studies. Here, indicate whether each material, system or method listed is relevant to your study. If you are not sure if a list item applies to your research, read the appropriate section before selecting a response.

Materials & experimental systems

n/a	Involved in the study
☒	☐ Antibodies
☒	☐ Eukaryotic cell lines
☒	☐ Palaeontology and archaeology
☒	☐ Animals and other organisms
☒	☐ Clinical data
☒	☐ Dual use research of concern
☒	☐ Plants

Methods

n/a	Involved in the study
☒	☐ ChIP-seq
☒	☐ Flow cytometry
☐	☒ MRI-based neuroimaging

Magnetic resonance imaging

Experimental design

Design type	Structural and resting-state fMRI.
Design specifications	NA; active fMRI tasks were not used in this study.
Behavioral performance measures	NA; active fMRI tasks were not used in this study.

Acquisition

Imaging type(s)	Structural 3D T1-weighted and resting-state sequences.
Field strength	1.5 - 3 T.
Sequence & imaging parameters	Scanning protocols followed by each center are detailed in the Supplementary Information Table S8 and Table S9.
Area of acquisition	Whole-brain.

Diffusion MRI ☐ Used ☒ Not used

Preprocessing

Preprocessing software	Structural MRI scans were preprocessed using the DARTEL Toolbox for VBM2 using the Statistical Parametric Mapping software (SPM12, https://www.fil.ion.ucl.ac.uk/spm/software/spm12/). Resting-state fMRI images were preprocessed using the Data Processing Assistant for Resting-State fMRI toolbox (DPARSF v.4.4, http://rfmri.org/DPARSF), an open-access toolbox that generates an automatic pipeline for fMRI analysis. DPARSF works by calling the SPM and the Resting-State fMRI Data Analysis Toolkit (REST v.1.7).
Normalization	Structural MRI data: First, T1-weighted images in native space were segmented using the default parameters of the SPM12 (bias regularization was set to 0.001, and bias full-width at half-maximum-FWHM was set to 60-mm cut-off) into grey matter, white matter, and cerebrospinal fluid (these three tissues were used to estimate the total intracranial volume). Second, the 'DARTEL create template' module was run using the grey matter and white matter segmented images (SPM12 default parameters) to create a template generated from the entire dataset. This procedure increases the accuracy of intersubject alignment. Third, we used the 'Normalize to MNI Space' module (DARTEL Tools) for affine registration of the last template from the previous step into the MNI space. Such transformation was applied to all individual grey matter maps. Fourth, images were modulated to correct volume changes by Jacobian determinants and to avoid bias in the intensity of an area due to its expansion during warping. Finally, data were smoothed using a 10-mm FWHM isotropic Gaussian kernel to accommodate intersubject anatomical differences. The size of the kernel was selected based on previous recommendations. Resting-state fMRI data: Images were normalized to the MNI space using the echo-planar imaging template from SPM12, smoothed using an 8-mm full-width-at-half-maximum isotropic Gaussian kernel, and bandpass filtered between 0.01 and 0.08 Hz to correct and remove low-frequency drifts from the scanner.
Normalization template	Standard MNI (as implemented in SPM12).
Noise and artifact removal	Resting-state fMRI data: The first five volumes of each participant's resting-state recording were discarded to ensure that magnetization achieved a steady state. Images were slice-timing corrected (using the middle slice of each volume as the reference scan) and realigned to the first scan of the session to correct for head motion (SPM12 functions). We regressed out six motion parameters, cerebrospinal fluid, and white matter signals to reduce potential effects of motion and physiological artifacts such as cardiac and respiration effects (REST v.1.7 toolboxes). Motion parameters were estimated during realignment, and cerebrospinal fluid and white matter masks were derived from the tissue segmentation of each subject's T1 scan in native space with SPM12 (after co-registration of each subject's structural image with the functional image).
Volume censoring	We did not use volume censoring. No participant showed movements greater than 3 mm or rotations higher than 3º (group statistics can be found in Table S10).

Statistical modeling & inference

Model type and settings	Seed based functional connectivity.
Effect(s) tested	Connectivity strength (Pearson correlation coefficient).

Specify type of analysis: ☐ Whole brain ☒ ROI-based ☐ Both

Anatomical location(s)	For structural MRI, we used the AAL atlas. For functional connectivity, two bilateral seeds were placed on cubic regions of interest (voxel size = 7x7x7) for each network: the dorsal anterior cingulate cortex for the salience network, MNI coordinates 10, 34, 24 and -10, 34, 24; the posterior cingulate cortex for the default mode network, MNI coordinates 3,-54, 27 and -3,-54, 27; the middle frontal gyri for the executive network, MNI coordinates 30, -2, 62 and -30, -2, 62; the primary visual cortex for the visual network, MNI coordinates 8, -92, 8 and -8, -92, 8; and the primary motor cortex for the motor network, MNI coordinates 32, −30, 68 and -32, -30, 68. The Pearson correlation coefficient between the averaged BOLD signal of each pair of seeds and voxels comprised in standard masks typically involved in each resting-state network was used to extract one feature per network for each participant.

Statistic type for inference

(See Eklund et al. 2016)

NA; fMRI features were extracted to include into support vector regression models (see Study description).

Correction

NA; fMRI features were extracted to include into support vector regression models (see Study description).

Models & analysis

n/a	Involved in the study
☒	☐ Functional and/or effective connectivity
☒	☐ Graph analysis
☒	☐ Multivariate modeling or predictive analysis