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Reporting Summary

Nature Research wishes to improve the reproducibility of the work that we publish. This form provides structure for consistency and transparency in reporting. For further information on Nature Research policies, see our <u>Editorial Policies</u> and the <u>Editorial Policy Checklist</u>.

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	Cor	firmed	
\boxtimes		The exact sample size (n) for each experimental group/condition, given as a discrete number and unit of measurement	
	\boxtimes	A statement on whether measurements were taken from distinct samples or whether the same sample was measured repeatedly	
	\boxtimes	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.	
	\boxtimes	A description of all covariates tested	
	\boxtimes	A description of any assumptions or corrections, such as tests of normality and adjustment for multiple comparisons	
	\boxtimes	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)	
\boxtimes		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.	
\boxtimes		For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings	
\boxtimes		For hierarchical and complex designs, identification of the appropriate level for tests and full reporting of outcomes	
\boxtimes		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 <u>availability of computer code</u>
Data collection
Data was captured with software from the Achievement Platform, available as a mobile application for both Android and iOS operating

systems, with functionality to connect consumer mobile devices and third-party digital diary apps, as well as enable users to participate and engage in clinical research efforts

Data analysis	Analysis was conducted with Python 3 and the R statistical analysis software
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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 Research guidelines for submitting code & software for further information.

Data

Policy information about availability of data

All manuscripts must include a <u>data availability statement</u>. This statement should provide the following information, where applicable: - Accession codes, unique identifiers, or web links for publicly available datasets

- Accession codes, unique identifiers, or web links for publicly availab
 A list of figures that have associated raw data
- A list of ingures that have associated raw data
 A description of any restrictions on data availability

Qualified researchers may request access to data and related study documents including the study report, study protocol with any amendments, statistical analysis plan, and dataset specifications. Further details on Sanofi's data sharing criteria, eligible studies, and process for requesting access can be found at: https://www.clinicalstudydatarequest.com/.

Field-specific reporting

Please select the one below that is the best fit for your research. If you are not sure, read the appropriate sections before making your selection.

K 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

Life sciences study design

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

Sample size	 We powered the study to detect relevant differences in behavioral features within constipation windows as compared to non-constipation windows. We make the following two assumptions First, (conservatively) each participant experiences one constipation episode over the study window, and as such has an associated "pair" of constipation to non-constipation observations. Second, each behavioral feature has a 25% change in feature means between paired constipation vs non-constipation windows. This percentage change was selected as an approximate heuristic based on the observed difference in feature means across reported constipation severity levels as observed in the previous CHC Coco Consumer study. Note that this percentage change typically corresponds to a small to moderate effect size, and falls into the range of differences typically observed in features exhibiting meaningful separation of classes for use within a prediction task. Utilizing a previous population of individuals with self-reported constipation (CHC Coco Consumer Outreach), we computed the mean and standard deviation of each of the 500+ behavioral and physiological features contained within the Evidation feature library (as of spring 2018 when the powering was conducted). For each feature, we then compute the sample size required to achieve a power of 0.8, with a type I error rate of 0.05, adjusted using the Bonferroni correction to control the family-wise error rate. Using these univariate power calculations, we then select the sample size required to detect 90% of differences across all features. All calculations were done using the R statistical computing language. The proposed sample size of 1,500 accounts for 30% loss to follow up (based on previous experience with Evidation-run studies) throughout the study period.
Data exclusions	After completing informed consent, 1,572 participants (85.5%, 1572/1839) completed the final steps required for enrollment, completion of baseline assessment and connection of a Fitbit device, and were then enrolled into the study. Of those, 32 participants did not complete any of the daily surveys, and were removed, leaving 1,540 enrolled persons in the analysis. Analysis of management approaches for constipation was conducted on those individuals who completed all the monthly surveys (n = 1,293 or 82% of enrolled), while the behavioral activity analysis was performed on those individuals who satisfied the previously described data density criteria (n = 756 or 48% of enrolled). The behavioral analysis population was determined as all enrolled participants with a multi-step process that includes the following [Tudor-Locke 2012, Migueles 2017]: 1. Estimate Fitbit wear time (in hours) for each user based on available minute-level data extracted from the Fitbit device, 2. Any day with wear time < 10 hours will be labeled as an invalid day, and 3. Removal of all individuals with ≥ 7 consecutive invalid days. The enrolled (Monthly) population will be defined as all enrolled participants who completed at least one monthly survey.
Replication	Not applicable
Randomization	Not applicable
Blinding	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

Methods

n/a	Involved in the study	n/a	Involved in the study
	Antibodies		ChIP-seq
	Eukaryotic cell lines		Flow cytometry
	Palaeontology and archaeology		MRI-based neuroimaging
	Animals and other organisms		
	Human research participants		
	Clinical data		
	Dual use research of concern		
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Antibodies

Antibodies used	Describe all antibodies used in the study; as applicable, provide supplier name, catalog number, clone name, and lot number.
Validation	Describe the validation of each primary antibody for the species and application, noting any validation statements on the manufacturer's website, relevant citations, antibody profiles in online databases, or data provided in the manuscript.

Eukaryotic cell lines

Policy information about <u>cell lines</u>		
Cell line source(s)	State the source of each cell line used.	
Authentication	Describe the authentication procedures for each cell line used OR declare that none of the cell lines used were authenticated.	
Mycoplasma contamination	Confirm that all cell lines tested negative for mycoplasma contamination OR describe the results of the testing for mycoplasma contamination OR declare that the cell lines were not tested for mycoplasma contamination.	
Commonly misidentified lines (See ICLAC register)	Name any commonly misidentified cell lines used in the study and provide a rationale for their use.	

Palaeontology and Archaeology

Specimen provenance	Provide provenance information for specimens and describe permits that were obtained for the work (including the name of the issuing authority, the date of issue, and any identifying information).	
Specimen deposition	Indicate where the specimens have been deposited to permit free access by other researchers.	
Dating methods	If new dates are provided, describe how they were obtained (e.g. collection, storage, sample pretreatment and measurement), where they were obtained (i.e. lab name), the calibration program and the protocol for quality assurance OR state that no new dates are provided.	
Tick this box to confirm that the raw and calibrated dates are available in the paper or in Supplementary Information.		
Ethics oversight	Identify the organization(s) that approved or provided guidance on the study protocol, OR state that no ethical approval or guidance was required and explain why not.	

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

Animals and other organisms

Policy information about studies involving animals; ARRIVE guidelines recommended for reporting animal research			
Laboratory animals	For laboratory animals, report species, strain, sex and age OR state that the study did not involve laboratory animals.		
Wild animals	Provide details on animals observed in or captured in the field; report species, sex and age where possible. Describe how animals were caught and transported and what happened to captive animals after the study (if killed, explain why and describe method; if released, say where and when) OR state that the study did not involve wild animals.		
Field-collected samples	For laboratory work with field-collected samples, describe all relevant parameters such as housing, maintenance, temperature, photoperiod and end-of-experiment protocol OR state that the study did not involve samples collected from the field.		
Ethics oversight	Identify the organization(s) that approved or provided guidance on the study protocol, OR state that no ethical approval or guidance was required and explain why not.		

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

Human research participants

Policy information about studies involving human research participants

Population characteristics	Of the 1,540 enrolled participants, mean age 36.6, and mostly female (72.8%), Caucasian (88.8%) and well educated (69.6% with at least a college degree)
Recruitment	Participants were recruited from the Achievement Platform, described above, which numbers more than 3 million members.
Ethics oversight	The study was approved by Solutions Institutional Review Board (Yarnell, AZ, USA).

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

Clinical data

Policy information about clinical studies

All manuscripts should comply with the ICMJE guidelines for publication of clinical research and a completed CONSORT checklist must be included with all submissions.

Clinical trial registration	Provide the trial registration number from ClinicalTrials.gov or an equivalent agency.
Study protocol	Note where the full trial protocol can be accessed OR if not available, explain why.
Data collection	Describe the settings and locales of data collection, noting the time periods of recruitment and data collection.
Outcomes	Describe how you pre-defined primary and secondary outcome measures and how you assessed these measures.

Dual use research of concern

Policy information about dual use research of concern

Hazards

Could the accidental, deliberate or reckless misuse of agents or technologies generated in the work, or the application of information presented in the manuscript, pose a threat to:

No	Yes
\boxtimes	Public health
\boxtimes	National security
\boxtimes	Crops and/or livestock
\boxtimes	Ecosystems
\boxtimes	Any other significant area

Experiments of concern

Does the work involve any of these experiments of concern:

No	Yes
\boxtimes	Demonstrate how to render a vaccine ineffective
\boxtimes	Confer resistance to therapeutically useful antibiotics or antiviral agents
\boxtimes	Enhance the virulence of a pathogen or render a nonpathogen virulent
\boxtimes	Increase transmissibility of a pathogen
\boxtimes	Alter the host range of a pathogen
\boxtimes	Enable evasion of diagnostic/detection modalities
\boxtimes	Enable the weaponization of a biological agent or toxin
\boxtimes	Any other potentially harmful combination of experiments and agents

ChIP-seq

Data deposition

Confirm that both raw and final processed data have been deposited in a public database such as GEO.

Confirm that you have deposited or provided access to graph files (e.g. BED files) for the called peaks.

Data access links May remain private before publication.	For "Initial submission" or "Revised version" documents, provide reviewer access links. For your "Final submission" document, provide a link to the deposited data.
Files in database submission	Provide a list of all files available in the database submission.
Genome browser session (e.g. <u>UCSC</u>)	Provide a link to an anonymized genome browser session for "Initial submission" and "Revised version" documents only, to enable peer review. Write "no longer applicable" for "Final submission" documents.

Methodology

Replicates	Describe the experimental replicates, specifying number, type and replicate agreement.
Sequencing depth	Describe the sequencing depth for each experiment, providing the total number of reads, uniquely mapped reads, length of reads and whether they were paired- or single-end.
Antibodies	Describe the antibodies used for the ChIP-seq experiments; as applicable, provide supplier name, catalog number, clone name, and lot number.
Peak calling parameters	Specify the command line program and parameters used for read mapping and peak calling, including the ChIP, control and index files used.
Data quality	Describe the methods used to ensure data quality in full detail, including how many peaks are at FDR 5% and above 5-fold enrichment.
Software	Describe the software used to collect and analyze the ChIP-seq data. For custom code that has been deposited into a community repository, provide accession details.

Flow Cytometry

Plots

Confirm that:

The axis labels state the marker and fluorochrome used (e.g. CD4-FITC).

The axis scales are clearly visible. Include numbers along axes only for bottom left plot of group (a 'group' is an analysis of identical markers).

All plots are contour plots with outliers or pseudocolor plots.

A numerical value for number of cells or percentage (with statistics) is provided.

Methodology

Sample preparation	Describe the sample preparation, detailing the biological source of the cells and any tissue processing steps used.
Instrument	Identify the instrument used for data collection, specifying make and model number.
Software	Describe the software used to collect and analyze the flow cytometry data. For custom code that has been deposited into a community repository, provide accession details.
Cell population abundance	Describe the abundance of the relevant cell populations within post-sort fractions, providing details on the purity of the samples and how it was determined.
Gating strategy	Describe the gating strategy used for all relevant experiments, specifying the preliminary FSC/SSC gates of the starting cell population, indicating where boundaries between "positive" and "negative" staining cell populations are defined.

Tick this box to confirm that a figure exemplifying the gating strategy is provided in the Supplementary Information.

Magnetic resonance imaging

Expe	erime	ntal c	lesign	
			0	

Design type	Indicate task or resting state; event-related or block design.
Design specifications	Specify the number of blocks, trials or experimental units per session and/or subject, and specify the length of each trial or block (if trials are blocked) and interval between trials.
Behavioral performance measures	State number and/or type of variables recorded (e.g. correct button press, response time) and what statistics were used to establish that the subjects were performing the task as expected (e.g. mean, range, and/or standard deviation across subjects).

Acquisition

Imaging type(s)	Specify: functional, structural, diffusion, perfusion.	
Field strength	Specify in Tesla	
Sequence & imaging parameters	Specify the pulse sequence type (gradient echo, spin echo, etc.), imaging type (EPI, spiral, etc.), field of view, matrix size, slice thickness, orientation and TE/TR/flip angle.	
Area of acquisition	State whether a whole brain scan was used OR define the area of acquisition, describing how the region was determined.	
Diffusion MRI Used	Not used	
Preprocessing		
Preprocessing software	Provide detail on software version and revision number and on specific parameters (model/functions, brain extraction, segmentation, smoothing kernel size, etc.).	
Normalization	If data were normalized/standardized, describe the approach(es): specify linear or non-linear and define image types used for transformation OR indicate that data were not normalized and explain rationale for lack of normalization.	
Normalization template	Describe the template used for normalization/transformation, specifying subject space or group standardized space (e.g. original Talairach, MNI305, ICBM152) OR indicate that the data were not normalized.	

Describe your procedure(s) for artifact and structured noise removal, specifying motion parameters, tissue signals and Noise and artifact removal physiological signals (heart rate, respiration). Define your software and/or method and criteria for volume censoring, and state the extent of such censoring. Volume censoring

Statistical modeling & inference

Model type and settings	Specify type (mass univariate, multivariate, RSA, predictive, etc.) and describe essential details of the model at the first and second levels (e.g. fixed, random or mixed effects; drift or auto-correlation).	
Effect(s) tested	Define precise effect in terms of the task or stimulus conditions instead of psychological concepts and indicate whether ANOVA or factorial designs were used.	
Specify type of analysis: W	hole brain 🗌 ROI-based 🔲 Both	
Statistic type for inference (See <u>Eklund et al. 2016</u>)	Specify voxel-wise or cluster-wise and report all relevant parameters for cluster-wise methods.	
Correction	Describe the type of correction and how it is obtained for multiple comparisons (e.g. FWE, FDR, permutation or Monte Carlo).	

Models & analysis

n/a Involved in the study			
Functional and/or effective connectivity			
Graph analysis	Graph analysis		
Multivariate modeling or predictive analysis			
Functional and/or effective connectivity	Report the measures of dependence used and the model details (e.g. Pearson correlation, partial correlation, mutual information).		
Graph analysis	Report the dependent variable and connectivity measure, specifying weighted graph or binarized graph, subject- or group-level, and the global and/or node summaries used (e.g. clustering coefficient, efficiency, etc.).		
Multivariate modeling and predictive analysis	Specify independent variables, features extraction and dimension reduction, model, training and evaluation metrics.		