Mechanism for top-down control of working memory capacity

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Working memory capacity, the maximum number of items that we can transiently store in working memory, is a good predictor of our general cognitive abilities. Neural activity in both dorsolateral prefrontal cortex and posterior parietal cortex has been associated with memory retention during visuospatial working memory tasks. The parietal cortex is thought to store the memories. However, the role of the dorsolateral prefrontal cortex, a top-down control area, during pure information retention is debated, and the mechanisms regulating capacity are unknown. Here, we propose that a major role of the dorsolateral prefrontal cortex in working memory is to boost parietal memory capacity. Furthermore, we formulate the boosting mechanism computationally in a biophysical cortical microcircuit model and derive a simple, explicit mathematical formula relating memory capacity to prefrontal and parietal model parameters. For physiologically realistic parameter values, lateral inhibition in the parietal cortex limits mnemonic capacity to a maximum of 2–7 items. However, at high loads inhibition can be counterbalanced by excitatory prefrontal input, thus boosting parietal capacity. Predictions from the model were confirmed in an fMRI study. Our results show that although memories are stored in the parietal cortex, interindividual differences in memory capacity are partly determined by the strength of prefrontal top-down control. The model provides a mechanistic framework for understanding top-down control of working memory and specifies two different contributions of prefrontal and parietal cortex to working memory capacity.

Here, we provide a comprehensive mathematical account supported by neuroimaging data of the mechanism behind vsWM capacity, including the effects of top-down signals.

Results

Persistent-Activity Models Have Limited Capacity. To understand how capacity is reached as vsWM load increases, we used a computational model of vsWM in IPS composed of spiking neurons (23) (see Materials and Methods). The model consisted of excitatory pyramidal cells (E cells) and inhibitory interneurons (I cells), each coding for a stimulus location at a specific angle. All cells were interconnected and received nonspecific independent random inputs from other brain regions. Connections between E cells coding for nearby stimuli were stronger than average (Fig. L4), a requirement for memory (23). After the brief presentation of a stimulus array, memories were maintained through localized bumps of activity (clusters of neighboring cells with raised activity) that supported themselves through the strong connections between neighboring E cells (bump attractors, Fig. 1B). However, network capacity was limited; not all stimuli led to stable persistent activity bumps (Fig. 1B).

Lateral Inhibition Limits capacity. Networks could have different capacities depending on parameters defining external inputs, connection strength, and cellular physiology. Data in Fig. 1 C and D come from networks with capacity 1, 2, or 3 that differed in the amount of nonspecific random input they received. Fig. 1C shows neural activity averaged over the whole network, whereas Fig. 1D shows activity in activated memory populations and current into nonactivated populations. Regardless of network capacity, total E cell activity increased with increasing load, which in turn caused increased I cell activity (Fig. 1C). Notice that networks with higher capacity had slightly higher E cell and I cell activity at the same load. Whereas E cell activity resulted mainly in recurrent synaptic inputs into neighboring cells, inhibitory feedback was widely distributed to all E cells. Hence, each stimulus contributed a net inhibitory current into distant cells, so that synaptic current into cells not storing any memory declined with increasing vsWM load (Fig. 1D). Network capacity was then limited by this mounting inhibition because persistent activity in the network requires a minimal level of effective feedback excitation. At the group level (including networks of different capacity in a group analysis), this mechanism led to a sublinear relationship between activity and vsWM load that is similar to experimentally measured activity in IPS (9, 11, 12), including a dip in average network activity at supracapacity loads (Fig. 1E) (10–12).

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Mathematical Framework for WM Capacity. The computational model, in which the equations specifying neuronal and synaptic properties include significant biological detail, can only be studied numerically. However, by further developing a mean-field WM model (28, 29) that includes a set of simplifying assumptions (see Materials and Methods), we investigated capacity analytically. Through further model reduction, we could derive a single equation that relates mnemonic firing rates, $r$, to vsWM load, $p$, through synaptic and cellular parameters (Fig. 2 and Materials and Methods). In condensed form, it reads

$$ r = f([G^+ - G^- (p - 1)] r + I_X), $$

where $f$ is the neuronal input–output function relating rates to synaptic input, $G^+$ is the effective connection strength between neurons coding for the same stimulus (excitatory), $G^-$ is the effective connection strength between neurons coding for different stimuli (inhibitory), and $I_X$ is the nonspecific external input. Thus, $G^+ - G^- (p - 1)$ represents the effective recurrent connection strength for active populations in the network. These parameters are in turn determined by a number of underlying physiological parameters such as I cell→E cell connectivity, etc. (see Materials and Methods).

Persistent activity is possible when there is a solution such that the left and right sides of Eq. 1 equal each other, i.e., when the cellular activity that is fed back into the network (right side of Eq. 1) is strong enough to reproduce itself (left side of Eq. 1) (Fig. 2A). One can further derive a potential energy landscape (see Materials and Methods) that gives an intuitive understanding of how neural populations enter the memory state (Fig. 2B) and how stability is affected by changes in connectivity and external input parameters (Fig. 2C).

Based on Eq. 1, it was possible to find an explicit capacity equation

$$ p_{cap} = 1 + [G^+ - H(I_X)]/G^-, $$

where $H$ is the neuronal input–output function relating rates to synaptic input, $G^+$ is the effective connection strength between neurons coding for the same stimulus (excitatory), $G^-$ is the effective connection strength between neurons coding for different stimuli (inhibitory), and $I_X$ is the nonspecific external input. Thus, $G^+ - G^- (p - 1)$ represents the effective recurrent connection strength for active populations in the network. These parameters are in turn determined by a number of underlying physiological parameters such as I cell→E cell connectivity, etc. (see Materials and Methods).
where \( H(I_X) \) is the effective connection strength at capacity \( [G^+ - G^- (p_{\text{cap}} - 1)] \) as a function of \( I_X \), \( H(I_X) \), whose explicit form depends on \( f \), decreases monotonously with \( I_X \) but is limited below by the inverse of the maximal slope of \( f \) [see supporting information (SI) Fig. S1]. Thus, capacity \( p_{\text{cap}} \) is increased by strong local excitation \( (G^+) \), strong excitatory drive \( (I_X) \), and weak lateral inhibition \( (G^-) \); Fig. S2).

The compact form of Eq. 1 provides a parsimonious account of the mechanistic basis of capacity and is consistent with the simulation results (Fig. 1): as \( p \) increases, each active population contributes an incremental inhibitory conductance \( G^- \) to the rest of the network. This progressively destabilizes the memory state, which eventually disappears when capacity is exceeded (Fig. 2 D and E).

**Inhibition Limits Capacity to a Few Items Only.** An important question is why vsWM capacity is limited to \( \approx 4 \) items. As outlined in the SI Appendix, an upper limit \( p_{\text{cap}}^U \) for the capacity can be derived:

\[
p_{\text{cap}}^U = \frac{1}{w} \left( 1 - (1 - w) \frac{H(I_X)}{G_{\text{max}}} \right)
\]

Here, \( w \) is the size of a neural population coding for a single item relative to the whole network, and \( G_{\text{max}} \) is the maximum excitatory connection strength for which the quiescent state of the network is stable. Given the constraints on spontaneous and persistent activity stability and the \( f\)-I curve of cortical neurons, we find that \( G_{\text{max}}/H(I_X) < 1.5 \) (Fig. S3) and \( p_{\text{cap}}^U \) is limited to a fraction \( (\approx 40\%) \) of the total number of coding populations \( 1/w \) (see SI Appendix). Experimentally, we still lack a clear estimation for \( w \) in vsWM, but recent estimates from delayed match-to-sample tasks in monkeys lie between 0.05 and 0.25, depending on the area (33). Taking these values, our model predicts that inhibition mechanisms numerically constrain vsWM capacity within a range of 2–7 items. The match with experimentally measured capacity suggests that inhibition can be a major mechanism underlying vsWM capacity.

**Lateral Inhibition Explains Supracapacity Performance Deterioration and Brain Activation Decreases.** The lateral inhibition mechanism explains the experimentally observed, sublinear relationship between load and activity (9, 11, 12), even including the supracapacity activity dip (10–12) (Fig. 1D). In experiments, a supracapacity dip in average group activity occurs even though the mean number of encoded items in the group of participants plateaus at supacapacity loads and remains relatively constant (11). Models with inhibition-limited capacity contain mechanisms that explain these findings. A key observation here is that although the mean number of stored items remains constant, interindividually variability increases, implying that high-capacity participants store additional items whereas low-capacity participants store fewer (9, 11). The energy formulation can explain why the farther above capacity the load is, the fewer stimuli are stored. At supracapacity loads, bumps become unstable. Because of noise, some bumps decay faster than others. After their disappearance, the remaining bumps recover (Fig. 2E). At high loads, the energy landscape is steeper, so more bumps disappear before the landscape restabilizes, and the model stores even fewer stimuli (Fig. 2F). In a population of participants with a range of capacities, the average number of stored items will remain constant, whereas its variance will increase with load: low-capacity individuals store fewer and high-capacity individuals more items as load is increased. This has been observed in behavioral experiments: when load increases above 3 items, the group mean number of stored items plateaus, but interindividually variability increases (9, 11).

Furthermore, lateral inhibition can also explain why the plateau in behavior leads to a dip in group brain activity. Lateral inhibition causes mnemonic rate to decrease with load (Figs. 1D and 2E). Assuming a linear decrease, \( a - bx \), where \( x \) is the number of stored items, total network activity is \( z = a(x - bx) \). Assume a distribution \( f(x; \mu, \sigma^2) \) of \( x \) among the participants with mean \( \mu \) and variance \( \sigma^2 \). Then the population IMRI activity equals \( f(x; \mu, \sigma^2) z dx = f(x; \mu, \sigma^2) (x(a - bx)) dx = a\mu - bE[x^2] = a\mu - b\mu^2 - b\sigma^2 \), where \( E[x] \) denotes the expected value. As discussed above, both our model and behavioral experiments indicate that for loads beyond the mean group capacity, the group mean of stored items \( \mu \) is constant and its variance \( \sigma^2 \) increases. This means that group activity \( a\mu - b\mu^2 - b\sigma^2 \) decreases above the group’s capacity, thereby producing the dip.

**Boosting of WM Capacity Through dlPFC Top-Down Excitation.** The fact that capacity is affected by the amount of external current entering the network \( I_X \) suggests that network capacity could be dynamically controlled by other brain regions, such as the dlPFC. To test this, we modeled dlPFC signals as an excitatory current injected into all E cells. Fig. 3A and B shows simulations with and without dlPFC signals. The nonspecific dlPFC input counteracts the growing lateral inhibition, thereby dynamically boosting the intrinsic capacity of IPS (Fig. 3C and D). This represents a specific way in which dlPFC top-down signals control vsWM: general excitation of attractor WM networks boosts their capacity. The mechanism can be understood graphically from Fig. 2D. At high loads, the input–output and synaptic functions cease to overlap (memory state is lost). Increased top-down excitation restores its stability (the overlap reappears). We propose that boosting of capacity through nonspecific top-down excitation is a neural mechanism for prefrontal top-down control of WM.

If capacity can be improved dynamically by using valuable dlPFC resources, why not instead start out with IPS having optimal capacity (through optimization of \( f \), \( G^+ \), \( G^- \), and \( I_X \))?
significant likelihood of detecting functional interregional interactions. We restricted further analysis to ipsilateral regions to increase the significant bilateral activations (analyzed in this study (14). The distracter task was not (Fig. 4).

Methods
achieve better performance in high-load trials. (iv) The frontal brain areas that activated significantly either in the M5–C5 or M3–C3 contrast conjunction (Table S1) were dlPFC (a), SFG (b), IFG (c), and mSFG (d). Based on a priori knowledge, we identified clusters in the visual cortex (e) and the load-dependent IPS area (f). (C) Correlation between the M5–M3 activity contrast in dlPFC and IPS (n = 25). (D) Correlation between M5–M3 performance drop and dlPFC activity (n = 21).

Fig. 3E shows that parameter changes that increased capacity also increased the risk of spontaneous memories at low loads. Thus, the optimal use of neural resources would be to activate dlPFC selectively at high loads. The maximal activity of dlPFC would then set the capacity of the entire frontoparietal network.

Neuroimaging Data Support Model Predictions. The model makes four predictions: (i) Individuals with strong dlPFC activation achieve better performance in high-load trials. (ii) Interindividual IPS and dlPFC activity correlations should be higher at high than low loads because capacity boosting is more important. Hence, (iii) dlPFC activity and performance should be more strongly correlated for high-load than low-load trials, whereas (iv) IPS activation and task performance should correlate equally well at all loads (because memories are stored there).

To test these predictions, we analyzed brain activity from 25 healthy adults (behavioral data were analyzed from 21 participants) whose brain activity had been measured with fMRI during the performance of a vsWM task (14) (see Materials and Methods). There were two tasks, M3 and M5, in which participants had to remember the location of 3 or 5 dots, respectively (Fig. 4A). In addition, there were two control tasks (C3, C5) with identical visual stimulation as the memory tasks, and a distracter task with the same stimuli as in M5. The distracter task was not analyzed in this study (14).

To find vsWM control regions, we conducted a whole-brain conjunction analysis (see Materials and Methods) to find regions activated in either the M3–C3 or M5–C5 contrasts and found significant bilateral activations (P < 0.05) in areas of the occipital, parietal, and frontal cortices (Table S1 and Fig. 4B). We also defined a parietal cluster with a significant M5–M3 contrast (P < 0.05; Fig. 4Bb) within the reported load-dependent region in the right hemisphere (9, 14) (see Materials and Methods), and we restricted further analysis to ipsilateral regions to increase the likelihood of detecting functional interregional interactions. We especially focused on dlPFC (Fig. 4Ba). We noted that the difference in activity between M5 and M3 trials in dlPFC was not significant (P = 0.11, n = 25). This suggests that not all participants used increased top-down boosting in high-load trials. However, those participants whose M5–M3 dlPFC contrast was above average (n = 9) performed significantly better in M5 trials than the other participants (n = 12) (79 ± 2% vs. 65 ± 5% correct trials; mean ± SEM; P = 0.015). The two groups did not differ in performance on M3 trials (84 ± 3% vs. 87 ± 3% correct trials; mean ± SEM; P = 0.73). This confirms our prediction i). In addition, we found that our experimental data indicated that dlPFC boosting was not just sufficient but also necessary for good high-load performance. When considering those participants performing above average (n = 10, average 71% correct) in the M5 trials, their dlPFC activations in the M5–M3 contrast were significantly larger than in the below-average performing individuals (P = 0.02) and were significantly positive (P = 0.02).

To further investigate whether dlPFC could be responsible for capacity boosting in IPS, we then tested predictions ii–iv). Our data revealed strong dlPFC–IPS correlations during both M5 (Fig. 4C; R = 0.86, P < 0.001, n = 25) and M3 trials (R = 0.64, P < 0.001, n = 25). However, the correlation during M5 trials was significantly higher (P = 0.034). This could not be explained by different sensory stimulation because dlPFC–IPS correlations remained significantly higher in M5 than C5 trials (R = 0.03) but not in M5 than C5 trials (R = 0.9). The increased dlPFC–IPS correlation was therefore specifically associated with high-load mnemonic trials, confirming prediction ii). This enhanced correlation had a behavioral consequence: the correlation between the dlPFC M5–M3 contrast and the M5–M3 performance difference was significant (Fig. 4D; R = 0.57, P = 0.007, n = 21), whereas the correlation between the dlPFC M3 activation and M3 performance did not reach significance (R = 0.39, P = 0.08), confirming prediction iii). The difference between the two correlations was positive but did not reach significance (P = 0.25), perhaps because of the small sample size. Furthermore, participants with strong IPS activations tended to show high performance in both M3 and M5 trials (correlation IPS activity–performance M3: R = 0.44, P = 0.044; correlation IPS activity–performance drop M5–M3: R = 0.47, P = 0.03; n = 21; prediction iv).

We performed several further controls. We repeated our correlation analyses, replacing dlPFC by the other areas in Fig. 4B (areas b–e). Visual cortex and IFG behaved similarly to each other. Their activation correlated well with IPS activation (R > 0.4, P < 0.05, n = 25), but not with behavior (R < 0.05, P > 0.8, n = 21), irrespective of load. Superior frontal gyrus (SFG) activity correlated with IPS activity and behavior equally strongly for both low and high loads (M5: R_SFG-IPS = 0.69, P < 0.001, n = 25; R_SFG-performance drop = 0.39, P = 0.08, n = 21; M3: R_SFG-IPS = 0.49, P = 0.01, n = 25; R_SFG-performance = 0.46, P = 0.03, n = 21), indicating a tight coupling between IPS and SFG for vsWM maintenance (27), without a specific SFG implication in top-down control. The medial SFG (mSFG) cluster showed a pattern of correlations similar to the dlPFC cluster. mSFG correlated significantly more with IPS during M5 than M3 trials (M5: R = 0.84, P = 0.001; M3: R = 0.49, P = 0.01; difference test P = 0.01), and its activation correlated with behavior in the M5–M3 contrast (R = 0.49, P = 0.02), but not in the M3 contrast (R = 0.3, P = 0.2).

Discussion
In summary, we formulated a biophysically explicit computational model that, together with a conceptually comprehensive mathematical analysis, explains the limited capacity (2–7 items) of WM networks and formulates a new role for dlPFC in boosting the vsWM capacity of parietal circuits. Unspecific excitatory inputs onto the parietal network counteract capacity-setting lateral inhibitory interactions between stored memories (bump attractors) and thus allow higher vsWM capacity. Our fMRI data confirmed predictions from the model and support the idea that enhanced functional coupling between dlPFC and
IPS during high vsWM load boosts performance and is an important determinant of interindividual capacity differences.

Interestingly, despite the importance of dlPFC for capacity, all architectural complexity resides in the circuitry of IPS (tuned connectivity, parametric adjustments, inhibitory control, etc.), and dlPFC top-down signals remain mechanistically simple (unspecific excitatory inputs, which can be modeled as Poisson spike trains). This simplicity could allow dlPFC to exert top-down control in a large variety of cognitive tasks (34) without being overloaded with complexity.

It should be emphasized that although our hypothesis regarding top-down control concerned dlPFC, our model is not specific for that region, and boosting signals could also be provided by other regions. Indeed, our whole-brain fMRI analysis revealed that in addition to the middle frontal gyrus (Fig. 4Aa), the medial part of the superior frontal gyrus (mSFG; Fig. 4Bd), associated with regulation of dlPFC activity and response conflict (35), also exhibited a pattern of activity consistent with boosting.

The general validity of our results may depend on specific assumptions of our models. On the one hand, our IPS network simulations rely on nonoverlapping active neural pools, i.e., require a narrow connectivity (Fig. 1A Right). This is a constraint for our model that could be circumvented by replacing our ring model with multiple mutually inhibiting ring models with broader connectivity. Because of limited spatial resolution, current fMRI cannot differentiate between these two network architectures, and the degree of overlap of simultaneously active spatial memories in the IPS remains to be explored experimentally. Such population overlap could be an additional source of capacity limitation, alongside the inhibition mechanisms analyzed here. Another question is whether our results generalize to other available working memory models: object–WM models (28) and models where memories are stored in different phases of a θ oscillation cycle (36). Object–WM models share mechanisms for memory stability with the vsWM model (general inhibition but strong local excitation) and differ only in connectivity architecture. Our results generalize to that model, as evidenced by our object–WM mean-field analysis. However, the effects of top-down inputs on the model based on θ oscillations (36) cannot be inferred from our results and remain to be studied separately.

Our results have implications for the discussion on the relation between capacity and brain activity. With physiologically plausible model parameters, lateral inhibition leads to an upper bound for capacity of 2–7 items, which is similar to experimentally measured capacity. Furthermore, the model shows that parietal networks with higher capacity generally have higher activity than low-capacity networks at the same load (Fig. 1C and D and Fig. S2), as previous experiments have found (12, 27, 37). It also shows that stronger prefrontal inputs increase IPS activity and boost capacity (Fig. 3E and Fig. S2D), consistent with our fMRI data. In addition, the boosting mechanism is consistent with studies showing that dlPFC activates specifically at high loads (19, 38) and is more activated in people with high capacity (11, 37) and that transcranial activation of dlPFC improves WM performance (39). Finally, our model explains the dissociation of memory load effects in dlPFC and IPS, where IPS and not dlPFC activation declines at supracapacity memory loads (10–12).

There have been two explanations for interindividual differences in vsWM capacity: that it either results from differences in passive storage capacity (12) or that people differ in how efficiently they use this storage capacity for storing only behaviorally relevant items (14). The present results add another dimension to this discussion by showing that one of the effects of prefrontal top-down control is actually to increase the storage capacity. This suggests that we should think of vsWM capacity as consisting of at least two capacities: one prefrontal and one parietal.

Materials and Methods

Simulation Model. The model included two brain regions, IPS and dlPFC. The IPS network consisted of 1,024 excitatory (E cells) and 256 inhibitory (I cells) integrate-and-fire neurons, connected through conductance-based synapses of the AMPA, NMDA, and GABA<sub>A</sub> types (23). The network had a ring structure, where adjacent cells encoded stimuli at adjacent angles and fixed eccentricity from the point of eye fixation (Fig. 1A, details of model in ref 23). Connections between E cells were spatially tuned (Fig. 1A Right), such that nearby cells were strongly connected, whereas distant cells had relatively weaker connections (40). The connection strength g<sub>E-E</sub>(d, h) between E cells (d) and I cells (h) depends on the difference in preferred angle between the cells (Fig. 1A Right) and is described by the equation

\[
\begin{align*}
    g_{E-E}(d, h) &= G_{E-E} W_{E-E}(\theta_d - \theta_h), \\
    W_{E-E}(\theta_d - \theta_h) &= J_{E-E} + (J_{E-E} - J_{E-E}) e^{-(\theta_d - \theta_h)^2/\sigma^2_{E-E}},
\end{align*}
\]

where G is the mean, J the peak value, J' the minimum value, and σ the width of this Gaussian curve. J' is set so that ∫W dθ = 1. Connections also existed from E cells to I cells (AMPA and NMDA), I cells to E cells (GABA<sub>A</sub>), and I cells to I cells (GABA<sub>A</sub>). Because of the strong disynaptic connections via I cells, distant E cells effectively inhibited each other. The E cell–I cell and I cell–E cell connectivity also had a slight spatial tuning (41), but the connectivity was wider (σ<sub>E-I</sub> = σ<sub>I-E</sub> > σ<sub>E-E</sub>) and flatter (U<sub>E-I</sub> = U<sub>I-E</sub> = U<sub>E-E</sub>). The I cell–I cell connection was not spatially tuned, i.e., g<sub>I-I</sub>(d, h) = G<sub>I-I</sub>. In addition to recurrent connections, each cell in IPS also received input from the rest of the brain modeled as Poisson spike trains targeting AMPA synapses.

The dlPFC network was a source of persistent inhibitory signals into the IPS, similar to findings from neurophysiological experiments in monkeys (42). Because dlPFC just provided nonspecific, persistent excitatory currents to IPS, no specific assumptions about the internal connectivity of dlPFC were necessary. For simplicity, in Fig. 3A–C dlPFC had the same cells and synapses as IPS, but connections were not tuned. Therefore, whereas activity in IPS was spatially localized, dlPFC activated or inactivated globally. E cells in the dlPFC connected with excitatory AMPA connections to E cells and I cells in IPS. The net network effect of such top-down signals was excitatory. In Fig. 3D dlPFC was modeled as Poisson spike trains connected to IPS cells via AMPA synapses.

Visual stimuli entered at 0.5-s intervals into E cells in the IPS. For a stimulus at angle θ<sub>stim</sub>, the current into a cell coding for an angle θ was I<sub>E-E</sub>(0; θ<sub>stim</sub>) = α exp[I/μ(π/2)(θ<sub>stim</sub> − θ<sub>stim</sub>) − 1], where α = 0.025 nA, μ = 39. I<sub>E-E</sub>(0; θ<sub>stim</sub>) is similar to a Gaussian function with standard deviation 9.4°, centered at θ<sub>stim</sub> and maximal amplitude 0.39 nA. In Fig. 3A–C, a 0.1-°, 0.150-nA current was input to dlPFC from the time of stimulus presentation. This current caused dlPFC to enter the persistent-activity state. Stimulus strength into IPS or dlPFC did not affect capacity. The timing of this current was not important, as long as it occurred before the end of cue presentation.

Tables S2–S4 specify the parameters of the computational model that were not varied in the simulations. Table 55 specifies parameter variations for the figures.

Mean-Field Model. Overview. We generalized a previous mean-field model of object–WM (28, 29) to multiple simultaneous memories and made simplifications similar to those made in refs. 29 and 43 to condense the model to the single Eq. 1. Unlike the vsWM model used in simulations, memory-encoding populations in this model did not overlap, neither did memory activity have the possibility to become wider or narrower as in the vsWM model. The explicit calculations that led to Eqs. 1 and 2 can be found in the SI Appendix. The results from the analyses of the mean-field model generalized to the vsWM model, as verified by simulations.

Energy landscape formulation. For the graphical representation of the inhibition mechanism underlying capacity described in Fig. 2, we derived a potential energy function (minima represent local stable states, i.e., stable fixed points). An ad hoc dynamics for Eq. 1 was defined as d/dt = −r + f(G<sub>E</sub> − G<sub>I</sub>(P) + 1) r + k<sub>E</sub>, and the energy function E was defined from d/dt = −d/dr. We used the simplified input–output function f(θ) = 1/2(1 + e<sup>−θ/θ<sub>stim</sub></sup>) for E<sub>E</sub> = 22, G<sub>E</sub> = 2, k<sub>E</sub> = −6.25. E was computed numerically by using an adaptive Simpson quadrature algorithm in Matlab.

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MRI Data Acquisition and Analysis. The experiment, approved by the ethics committee of the Karolinska Hospital, was described in detail in ref. 14. Briefly, 25 healthy participants (age 19–33, right-handed, 13 females) were scanned in a 1.5 T GE Sigma scanner while performing the tasks in Fig. 4A. The various trials were randomly intermixed in an event-related design and were delivered in 4 sessions of 30 trials and duration of 7 min each. Button presses were recorded for all but one participant. For our behavioral analyses we also discarded 3 more participants, who had not completed all 4 scanning sessions. Their behavioral measures were based on few too trials to be reliable. Performance was significantly better for M3 than for M5 trials (86 ± 2% and 71 ± 3%, respectively, mean ± SEM, paired t test P < 0.0001, n = 21) and was equally high for the nonmnemonic tasks C3 and C5 (recorded for all but one participant. For our behavioral analyses we also acknowledged the resources and assistance from the Barcelona Supercomputing Center and the National Computer Centre in Linköping, Sweden. We thank C. Constantinidis, C. K. Machens, X.-J. Wang, E. Fransén, L. Nyberg, R. Moreno, and K. E. Stephan for comments on a previous version of the manuscript. F.E. was supported by a Ph.D. position from Kungliga Tekniska högskolan. A.C. acknowledges support from Instituto de Salud Carlos III, Ministerio de Ciencia e Innovación and Generalitat de Catalunya. T.K. was supported by the Royal Academy of Science and Knut and Alice Wallenberg Foundation. J.T. was supported by Foundation for Strategic Research, Wennergren Foundation, and Swedish Research Council.
