postsynaptic neuron. This then leads to activation of calcium-dependent protein kinases and NOS, which causes amplification of pain-related information at the first synapse in pain pathways. Blockade of IP_3Rs unmasked LTD of synaptic strength in C-fibers induced by LFS. This suggests that LFS may simultaneously induce synaptic plasticity of opposite polarity involving divergent signal transduction pathways. Hyperalgesia in human (*27*) and in animal studies (*7*, *28*, *29*) and the synaptic pain amplifier described in this work share induction mechanisms, relevant neuron populations in spinal cord, pharmacological profile, and signal transduction pathways. This strongly suggests that LTP at the first synapse in pain pathways between nociceptive C-fibers and spinal lamina I projection neurons is a cellular key mechanism of inflammatory hyperalgesia and perhaps other forms of low-level afferent-induced hyperalgesia (*30*, *31*).

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Food-Caching Western Scrub-Jays Keep Track of Who Was Watching When

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Western scrub-jays (*Aphelocoma californica*) hide food caches for future consumption, steal others' caches, and engage in tactics to minimize the chance that their own caches will be stolen. We show that scrub-jays remember which individual watched them during particular caching events and alter their recaching behavior accordingly. We found no evidence to suggest that a storer's use of cache protection tactics is cued by the observer's behavior.

Social living is suggested to have selected for increased sociocognitive skills in animals (*1*, *2*). Several species use information about the dominance rank (*3*) and social relationships (*4*) of conspecifics when forming alliances or competing for resources (*5*, *6*). Corvids rely on observational spatial memory to steal others' caches (*7*–*9*), and they engage in a variety of behaviors to reduce cache theft (*10*–*15*). It may be advantageous to remember who was watching during specific caching events, because scrub-jays can only defend caches against subordinates (*16*). Scrub-jays should therefore engage in cache protection when they are caching in view of dominant birds, but might refrain from doing so when watched by their partner, because they often defend their partner's caches and tolerate cache theft by their mate (*16*).

Nine birds (storers) cached in two trays, one near and one far from an observer. Storers cached in the presence of a dominant bird ("dominant"), a subordinate bird ("subordinate"), their partner ("partner"), or when an observer's view was obscured ("in private"). After 3 hours, storers recovered their caches "in private" (*17*). Partnerships and dominance indices were determined before this experiment when the birds were aviary housed (*16*).

The total number of items cached did not differ significantly between conditions [Friedman's analysis of variance (ANOVA), $\chi_3^2 = 2.5$, $P = 0.45$]. Birds cached predominantly in the far tray in the "dominant" (sign test: $S = 7/7$, $P = 0.02$) and "subordinate" condition ($S = 7/7$, $P = 0.02$), but not in the "partner" condition ($S = 5/7$, $P = 0.13$) or "in private" ($S = 3/7$, $P > 0.05$) (table S1).

The proportion of items that were recached at recovery was greatest in the "dominant" condition (Fig. 1A). In the "dominant" and "subordinate" conditions, items were predominantly moved from the near tray. Surprisingly, items were also moved, but from both trays, after the "in private" and "partner" conditions (Fig. 1B). Irrespective of condition, items were always moved to out-of-tray sites around the home cage.

The pattern of caching and recaching suggests that scrub-jays engage in cache protection to combat the specific risk that nonpartners pose to their caches, even though observers did not have the opportunity to pilfer. Specifically, birds cached mainly in the far tray when observed by a nonpartner and recached the few items hidden in the near tray at recovery. It may be difficult for observers to see the location of caches in the far tray, thereby decreasing their ability to use observational spatial memory to facilitate cache pilferage. This strategy was not implemented when the storer's partner was present, perhaps because storers prefer to spend time near to their partner and do not perceive them as a risk to cache safety.

There are three alternate explanations for the preference to cache in the far tray in the "dominant" and "subordinate" conditions.

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First, being near nonpartners might be aversive. However, in a previous experiment, scrub-jays spent similar amounts of time near and in-view and far and out-of-view of nonpartners during caching (*15*). Second, jays might be predisposed to cache at a distance from nonpartners. Yet our youngest cohort of birds do not discriminate between near [median = 1.5, interquartile range (IQR) = 11.5] and far trays (median = 6.5, IQR = 6.5; Wilcoxon's Z =0.42, P = 0.67) (table S4). Unlike the birds in this experiment (age 10), these young birds (age 3) have not experienced stealing others' caches, an experience that seems essential for the expression of recaching (*10*) and other protective behaviors. Finally, storers might have learned that caching in far sites reduces cache theft. However, storers received a single trial in each caching condition, and, because caches were never stolen, they received no feedback as to the success of their caching strategies. Critically, these explanations cannot explain the differences in the birds' recaching behavior, because cache recovery always occurred "in private." Differences in recaching must therefore be based on a storer's memory for the social status of who watched them cache.

To test whether scrub-jays remember which particular individual was present when they made specific caches, eight birds were given eight trials in which they cached successively in two trays, each in view of a different observer. Consequently, individual A observed the storer caching in one tray, and individual B observed the storer caching in a second tray immediately afterwards (AB trial), or vice versa (BA trial). During each caching period, both trays were placed in the storer's cage, but Perspex strips covered one tray to prevent caching in that tray. Observers therefore saw the storer caching in one (observed tray) but not the other tray. After 3 hours, storers recovered their caches either "in private," in-view of individual A or individual B ("observed" condition), or watched by a "control" bird that had not witnessed the storer caching (*17*). To control for any affect of observer social status on caching behavior, birds of similar rank were used, and storer-observer dominance relationships were counter balanced across trials.

No differences were detected in the number of items cached in the presence of individual A and individual B during AB and BA trials (χ_3^2 = 4.8, P = 0.21). The proportion of caches that were recached at recovery differed significantly between conditions (χ_3^2 = 17.9, $P < 0.01$) (table S2), and significantly more caches were recached during the "observed" condition relative to the "control" condition (Fig. 2A). A similar proportion of caches were recached from either tray "in private" ($S = 8/12$, P = 0.39), whereas in the "observed" condition, storers recached specifically from the "observed" tray (Fig. 2A). Few items were recached from the "other" tray in the "observed" condition, or from either tray in the "control" condition.

Recaching in the "observed" and "in private" conditions differed in two respects. First, "in private" items were recached in "out-of-

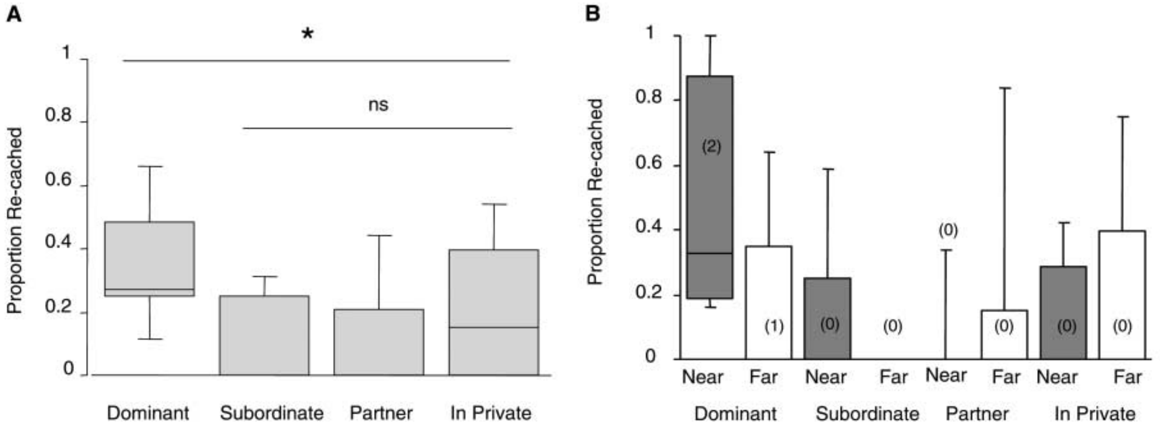
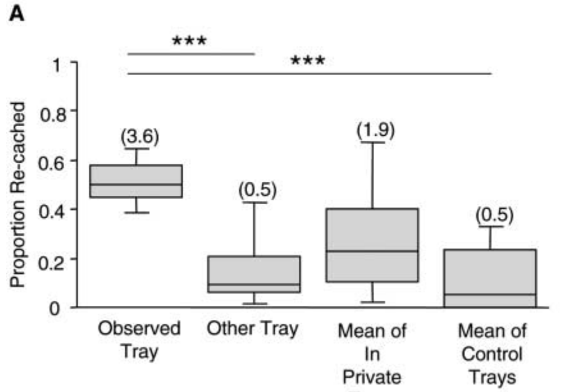


Fig. 1. Median proportion (25th percentile and 75th percentile) of items recached after each caching condition. (**A**) Recaching was greatest after the "dominant" condition (χ_3^2= 9.8, P = 0.02). When the "dominant" condition was removed from the analysis, no significant difference was identified between the remaining conditions (χ_3^2 = 1.4, P = 0.37). The asterisk indicates $P < 0.05$. ns, not significant. (**B**) The median proportion (25th percentile and 75th percentile) and median number (in parentheses) of items recached from "near" (open bars) and "far" (shaded bars) trays is shown for birds that cached in both trays. The data could not be analyzed statistically, because several birds did not cache in both trays (two in the "dominant" condition, four in the "partner" condition, and two "in private"), and their recovery behavior would therefore be confined to one location.



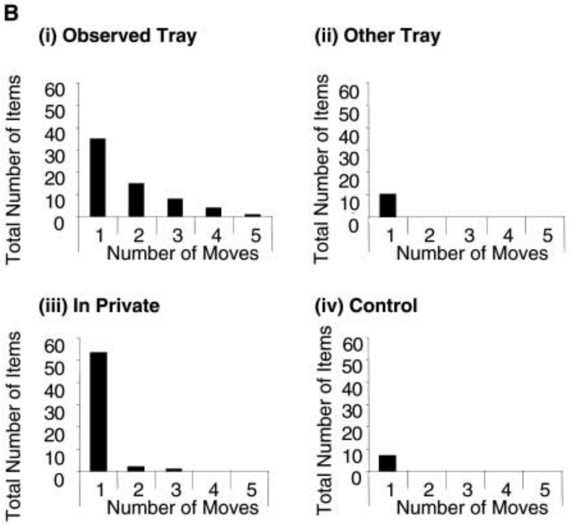


Fig. 2. (**A**) Median (25th percentile and 75th percentile) proportion and median number (in parentheses) of items recached from the "observed" and "other" trays in the "observed" condition, and the mean of trays in the "control" and "in private" conditions (χ_3^2 = 17.3, P = 0.0006). The proportion that was recached from the "observed" and "other" trays differed significantly ($S = 25/25$, $P < 0.001$). The triple asterisk indicates $P < 0.001$. (**B**) Total number of times items were moved from (i) the "observed" tray, (ii) the "other" tray, (iii) the "in private" trays, and (iv) the trays in the "control" condition. Caches in the "observed" tray were moved more often than caches in the "in private" trays (χ_1^2 = 8.0, P = 0.01). Recaching from the "other" tray and the trays in the "control" condition was too low to allow further analysis.

tray" locations. By contrast, items from the "observed" tray were predominantly moved to cache sites within that tray ($\chi_1^2 = 17.9$, $P < 0.01$) (table S2). Second, caches in the "observed" condition were moved twice as often as those recached "in private" (Fig. 2B). Repeatedly moving items may decrease the accuracy with which potential thieves can relocate caches, because memories for successive locations should interfere with one another. Storing jays have been shown to recover caches they did or did not move multiple times with a comparable degree of accuracy (*14*).

It is possible that in experiment 2, storers were simply reacting to cues provided by the observer (*18*). For example, observers may direct more (or less) attention to trays they have seen a bird caching in. In experiment 3, we repeated the "observed" condition of experiment 2, and contrasted it with an "observer-control" condition (Fig. 3A). The "observer-control" condition was identical to the "observed" condition, except that in the "observed" condition, the observer saw the same bird at caching and recovery, whereas in the "observer-control" condition, the control bird watched a different individual recover its caches from the one it saw caching (*17*).

If cache recovery is mediated by a memory for who was present during caching, the birds' recovery behavior should differ between the "observed" and "observer-control" conditions. Based on experiment 2, storers in the "observed" condition should recache predominantly from the tray in which the observer at recovery had seen them cache ("observed" tray). However, because the control bird was not present when the storer cached, few items should be recached from either tray in the "observer-control" condition. A behavior-cueing account leads to a different prediction. If observers primarily attend to trays in which they have seen caching, and if storers use these cues to guide recovery, then storers should recache specifically from the "observed" tray in both conditions.

The number of items cached in the "observed" and "observer-control" conditions did not differ statistically ($\chi_1^2 = 17.9$, $P = 0.86$), nor was there any preference for caching in either tray ("observed": $S = 7/14$, $P > 0.05$; "observer-control": $S = 7/12$, $P > 0.05$) (table S3). The proportion of caches that were recached at recovery did not differ statistically between conditions ($\chi_1^2 = 0.13$, $P = 0.72$). In the "observed" condition, items were predominantly recached from the "observed" and not from the "other" tray. By contrast, in the "observer-control" condition, items were recached from both trays without selectivity (Fig. 3B). In both conditions, few items were recached in "out-of-tray" sites ($\chi_1^2 = 8.1$, $P = 0.01$) (table S3). Furthermore, in terms of the behavior of the birds that were observing at recovery, there was no evidence that observers and control birds (that saw a different bird at caching and recovery) differed in the amount of time they spent nearest to, or oriented toward, either tray (*17*).

These results suggest that scrub-jays remember who observed them make specific caches, and are not consistent with a behavior-cueing account. In our experiments, observers were never given the opportunity to pilfer the storer's caches. However, in previous studies, the birds not only had their caches pilfered (*10*) but witnessed observers stealing their caches (*19*). The unpredictability of cache safety might have motivated storers to consistently engage in

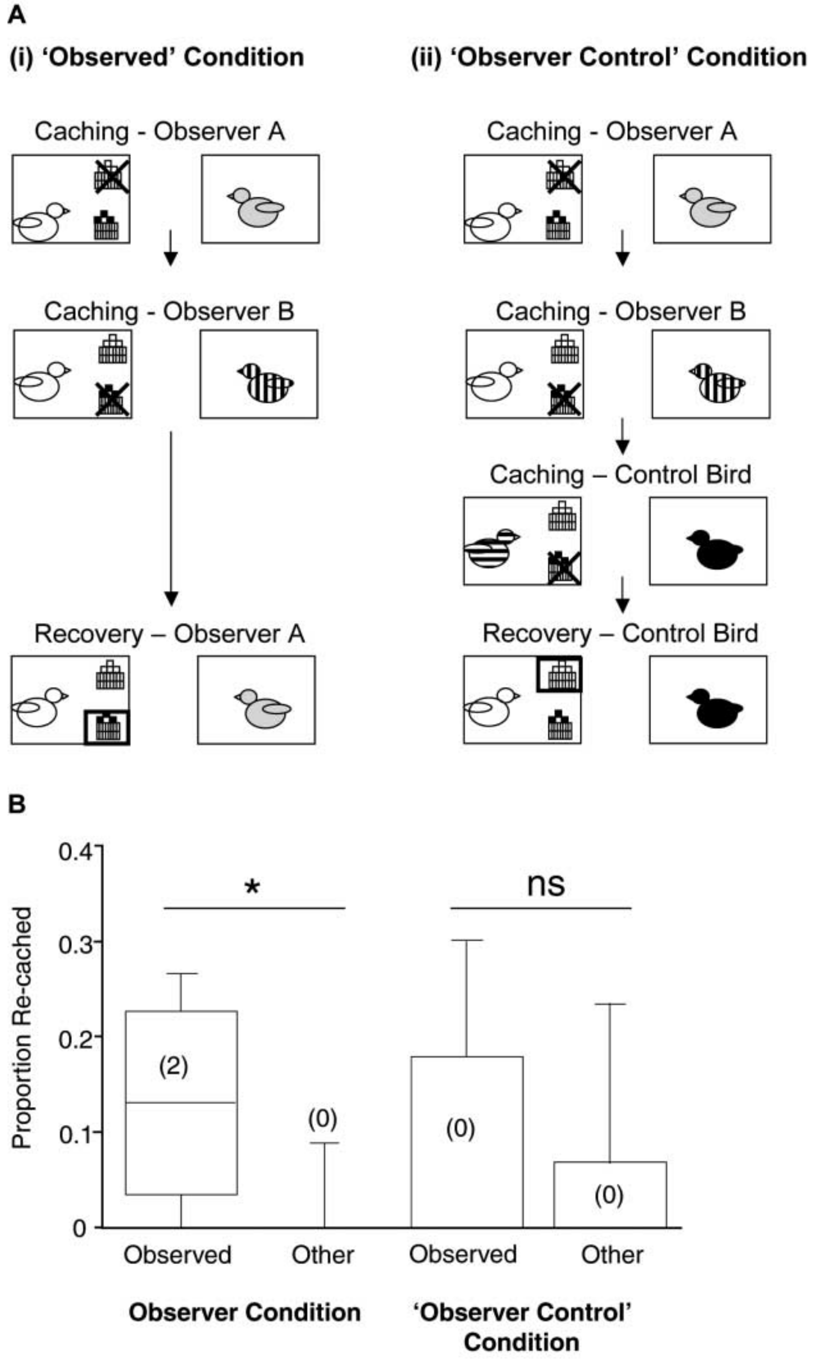


Fig. 3. (**A**) The "observed" and "observer-control" conditions of experiment 3. The clear bird indicates the storer in the "observed" and "observer-control" conditions, the horizontal striped bird indicates an additional storer in the "observer-control" condition, the lightly shaded bird indicates individual A, the vertical striped bird indicates individual B, and the black bird indicates the control bird. The black X indicates Perspex strips, the rectangle indicates the "observed" tray. (**B**) Median (25th percentile and 75th percentile) proportion and median number (in parentheses) of items recached from the "observed" and "other" trays in the "observed" ($S = 6/6$, $P = 0.03$) and "observer-control" conditions ($S = 4/6$, $P = 0.69$). The asterisk indicates $P < 0.05$. ns, not significant.

cache protection. Indeed, it was necessary to use different birds in experiments 2 and 3, because the birds in experiment 2 ceased to cache in the presence of an observer. Cache cessation appeared to be a direct consequence of observer presence as the birds continued to cache "in private," a finding perhaps indicative of a mechanism that acts to reduce caching levels with increased observer presence.

It is possible that scrub-jay caching and recovery behavior might be based on a series of conditional rules, rather than an assessment of risk. That is, jays might form specific associations between particular observers and cache locations. To generate the flexibility demonstrated in these experiments, however, these rules would have to be highly conditional and integrated with the associations between a specific tray and a particular individual.

Scrub-jays encode the "what-where-when" of specific caching episodes (*20*). Our findings suggest that scrub-jays also remember who was present during earlier caching events. This ability need not be based on a humanlike episodic memory, because these what-where-when memories may exist without the jay mentally reconstructing the past (*21*, *22*). Similarly, keeping track of who was watching when need not require a humanlike "theory-of-mind" in terms of attributing unobservable metal states (*18*), but it may result from behavioral predispositions in combination with specific learning algorithms or from reasoning about future risk.

The propensity for subordinates to adjust their behavior in response to the presence or absence of a dominant conspecific has been suggested as evidence for knowledge attribution in chimpanzees (*23*) and ravens (*24*). Although the ability of nonhuman animals to reason about another's mind continues to elude definitive study, our study provides evidence to suggest that a nonhuman animal might discriminate between individuals with different knowledge states.

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Regulation of B Cell Tolerance by the Lupus Susceptibility Gene *Ly108*

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The susceptibility locus for the autoimmune disease lupus on murine chromosome 1, *Sle1*^{z}/*Sle1b*^{z}, and the orthologous human locus are associated with production of autoantibody to chromatin. We report that the presence of *Sle1*^{z}/*Sle1b*^{z} impairs B cell anergy, receptor revision, and deletion. Members of the *SLAM* costimulatory molecule family constitute prime candidates for *Sle1b*^{z}, among which the *Ly108.1* isoform of the *Ly108* gene was most highly expressed in immature B cells from lupus-prone B6.*Sle1*^{z} mice. The normal *Ly108.2* allele, but not the lupus-associated *Ly108.1* allele, was found to sensitize immature B cells to deletion and *RAG* reexpression. As a potential regulator of tolerance checkpoints, *Ly108* may censor self-reactive B cells, hence safeguarding against autoimmunity.

Loss of B cell tolerance is the hallmark of systemic lupus erythematosus (SLE), or lupus, an antibody-mediated chronic autoimmune disease affecting multiple organs. However, the precise means by which tolerance is breached in lupus, and the underlying genes and molecules responsible, remain obscure. The origin of lupus in both mice and humans appears to be polygenic, involving more than a dozen potent loci (*1*–*3*), although of these, at least one locus on chromosome 1 appears to be shared by both species. The *z* allele of *Sle1* and its component sublocus *Sle1b*, derived from the lupus-prone NZM2410/NZW strain of mice, are linked to a variety of lupus-related disease phenotypes, including antinuclear antibodies (ANAs), splenomegaly, and glomerulonephritis (*4*, *5*). A locus on human chromosome 1 orthologous to murine *Sle1* has also been implicated in lupus susceptibility (*6*). Located within the *Sle1b*^{z} sublocus, the *SLAM* gene family–encoded costimulatory molecules are among the first candidate genes to be identified as being linked to spontaneous lupus in mice (*7*). Extensive polymorphisms and expression differences were documented in several members of this gene cluster between the normal C57BL/6 (B6) strain and the lupus-prone B6.*Sle1b*$^{z/z}$ congenic mice bearing the *z* haplotype of *SLAM* (*7*).

To determine the mechanisms by which B cell tolerance might be infringed in lupus, the B cell repertoire of B6.*Sle1*$^{z/z}$ congenic mice (*8*) was modified to an essentially monoclonal specificity by breeding onto them a B cell receptor (BCR) transgene specific for lysozyme (HEL) (*9*). In these B6.HEL^{Ig} mice, the HEL^{Ig} BCR transgene leads to a near-uniform pool of HEL-specific B cells bearing a BCR heavy chain of immunoglobulin M^{a} (IgM^{a}) allotype and high titers of serum antibodies to HEL of IgM^{a} allotype (*9*). Developmental exposure of these B cells to a strong cross-linking surrogate

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