Altered cognitive processes shape tactile perception in autism.

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Altered sensory perception is a hallmark of autism and determines how autistic individuals engage with their environment. These sensory differences are shaped by top-down cognitive processes—such as categorization, attention, and priors—which themselves exhibit characteristic atypicalities in the condition. Among sensory modalities, tactile perception is particularly critical for daily functioning and social interactions. However, the dynamic interplay between tactile and cognitive processes remains poorly understood.

In this study, we investigated the influence of top-down cognitive processes on tactile perception in the *Fmr1*$^{-/y}$ genetic mouse model of autism. We developed a translational, forepaw-based decision-making task designed to dissociate stimulus-driven tactile responses from those modulated by cognitive factors. This approach enabled us to assess multiple aspects of perceptual processing, including perceptual learning, stimulus categorization and discrimination, as well as the influence of prior experience and attention. Mice were initially trained to distinguish between high- and low-salience stimuli and were subsequently tested with a continuum of intermediate stimulus intensities.

Our results revealed salience-dependent cognitive alterations that significantly influenced sensory performance. During the training phase, *Fmr1*$^{-/y}$ mice exhibited an increased choice consistency bias in low-salience trials, resulting in impaired perceptual learning. In the testing phase, *Fmr1*$^{-/y}$ mice demonstrated enhanced tactile discrimination under low-salience conditions, driven by a reduced influence of categorization. Moreover, under conditions of high cognitive load, *Fmr1*$^{-/y}$ mice displayed attentional deficits that were dissociable from their enhanced tactile sensitivity. Together, our findings reveal that cognitive context critically shapes sensory phenotypes in autism. They advocate for a shift beyond traditional sensory–cognitive dichotomies to better capture the dynamic interplay between perceptual and cognitive alterations in autism.

Introduction

Autism is a neurodevelopmental condition that affects approximately 1 in 31 children (Shaw et al., 2025). Autistic individuals display differences in social interaction and communication, repetitive behaviors, intense or special interests, and altered sensory experience as core symptoms (American Psychiatric Association, 2022). Sensory alterations strongly affect the way autistic individuals interact with their environment. According to the DSM-5-TR, these are broadly expressed as "*hyper- or hyporeactivity to sensory input or unusual interests in sensory aspects of the environment*" and are reported in 90% of autistic individuals, spanning all sensory modalities (Robertson and Baron-Cohen, 2017).

Amongst sensory modalities, touch is the first sense to develop and plays a fundamental role in the exploration of the environment, the definition of "self", and early social bonding (Bremner and Spence, 2017). Tactile processing alterations have a significant impact on daily functioning and are thought to contribute to repetitive behaviors and social interaction difficulties in autism (Foss-Feig et al., 2012; Green et al., 2018; Thye et al., 2018; He et al., 2021a; Zhai et al., 2023; Carati et al., 2024).

Sensory perception is shaped not only by the physical properties of stimuli but also by top-down cognitive processes such as attention and categorization—both of which are altered in autism (Allen and Courchesne, 2001; Church et al., 2010; Gastgeb and Strauss, 2012; Cascio et al., 2015; Barbot et al., 2018; Rong et al., 2021a). Moreover, autistic individuals demonstrate differences in how prior beliefs and expectations (priors) are integrated with sensory input during perceptual decision-making. They tend to rely less on contextual priors (Amoruso et al., 2019) and more heavily on prior choices (Feigin et al., 2021), and often form priors that are imprecise or inflexible (Zaidel et al., 2015; Sapey-Triomphe et al., 2021b). Notably, variability in the use of priors has also been linked to individual differences in sensory responsivity (Sapey-Triomphe et al., 2021a). These cognitive differences may compound or interact with primary sensory processing alterations, contributing to the distinct perceptual experiences observed in autism.

Enhanced sensory processing—including heightened perceptual sensitivity, which is defined as improved ability to detect or discriminate stimuli (He et al., 2023)—has been proposed by several influential models of autism (Plaisted, 2001; Frith, 2003; Mottron et al., 2006) and supported by numerous studies in the visual and auditory domains (Plaisted et al., 1998a; O'Riordan and Plaisted, 2001; O'Riordan et al., 2001; Bonnel et al., 2003; O'Riordan and Passetti, 2006; Samson et al., 2006; Rotschafer, 2021). However, clinical studies focusing on tactile discrimination have yielded controversial results (Zetler et al., 2019), likely due to the substantial heterogeneity of tactile processing alterations in autism (Mikkelsen et al., 2018) and inconsistent terminology across studies (He et al., 2023).

Tactile discrimination of vibrotactile stimuli delivered to the glabrous skin of the fingers was reported reduced (Puts et al., 2014; Espenhahn et al., 2023), or intact (He et al., 2021a; Asaridou et al., 2022) in autistic individuals. Similarly, studies of sharp-dull discrimination have reported both reduced (Abu-Dahab et al., 2013) and typical performance (Minshew et al., 1997; Minshew and Hobson, 2008), as have studies of form discrimination (Minshew and Hobson, 2008; Demopoulos et al., 2015; Failla et al., 2017). Although these studies highlight the heterogeneity of tactile responses in autism, variability in experimental protocols and stimulus types has made it difficult to draw cohesive conclusions. Translational approaches employing mouse models of autism in combination with psychometric measures from well-controlled behavioral tasks may help clarify whether these inconsistencies reflect genuine inter-individual variability or arise from methodological differences.

While tactile discrimination has been explored in several clinical studies, it remains underexplored in mouse models of autism. Rodent studies leveraging innate responses have reported atypical whisker-dependent texture discrimination (Balasco et al., 2021, 2022; Mattioni et al., 2024) and forepaw-dependent roughness discrimination (Orefice et al., 2016). However, these studies have not employed psychophysical methods to quantify tactile discrimination, restricting the translatability of their findings. Implementing psychophysics in animal models might clarify previous inconsistencies between studies in mice (Orefice et al., 2016) and humans (O'Riordan and Passetti, 2006).

In this study, we investigated the interplay between tactile discrimination and cognitive processes during perceptual decision-making. To enhance translational relevance and address questions of inter-individual heterogeneity, we developed a forepaw-based 2-Alternative Choice task for mice, using vibrotactile stimuli analogous to those used in human psychophysical protocols. Leveraging this task, we explored how stimuli of varying salience are discriminated in the *Fmr1*$^{-/y}$ mouse model of autism and disentangled stimulus-driven- from cognitively modulated-tactile responses.

Our results revealed salience-dependent alterations in both tactile processing and cognitive modulation in *Fmr1*$^{-/y}$ mice, with a decreased top-down influence of cognitive processes on tactile perception. During the training phase, these mice exhibited impaired perceptual learning, driven by a heightened choice consistency bias in low-salience trials. After training, *Fmr1*$^{-/y}$ mice displayed intact choice bias but enhanced discrimination of low-salience stimuli. This enhancement was attributable to a decreased top-down influence of categorization on discrimination in *Fmr1*$^{-/y}$ mice. Furthermore, under high cognitive load, *Fmr1*$^{-/y}$ mice showed attention deficits that were dissociable from their tactile sensitivity. These findings uncover distinct, salience-dependent cognitive alterations that shape tactile perception in the *Fmr1*$^{-/y}$ model, advancing our understanding of tactile perception in autism. Importantly, our results indicate that the variability observed in clinical studies may arise not solely from primary sensory alterations but also from differences in cognitive context, attentional demands, or task complexity—offering a potential framework to reconcile prior inconsistencies in the field.

Results

Fmr1$^{-/y}$ mice show intact learning rate during perceptual learning.

To investigate perceptual and cognitive alterations in a highly translational approach using, we developed a forepaw-based 2-Alternative Choice perceptual decision-making task in the *Fmr1*$^{-/y}$ mouse model of autism. In this task, mice learn to discriminate between vibrotactile stimuli that differ in perceptual salience, which we define as the prominence of a stimulus based on its physical amplitude. To ensure that all mice could reliably detect the applied stimuli, we selected amplitudes above the perceptual thresholds previously established for both wild-type (WT) and *Fmr1*$^{-/y}$ mice (Semelidou et al., 2024). During each trial, head-fixed, water-controlled mice received a 500 ms vibrotactile stimulus to the forepaw—either high-salience (40 Hz, 26 µm) or low-salience (40 Hz, 12 µm). Mice were trained to report high-salience stimuli by licking the right lick-port, and low-salience stimuli by licking the left port within a 2-s response window. Incorrect choices resulted in a 5-s timeout (Fig. 1A).

Learning difficulties and altered learning trajectories have been reported in autistic individuals and replicated in several mouse models of autism, including *Fmr1*$^{-/y}$ mice (Arnett et al., 2014a; Goel et al., 2018; Mercado et al., 2020; Khachadourian et al., 2023; Shenouda et al., 2023; Mol et al., 2024). To assess whether *Fmr1*$^{-/y}$ mice exhibit alterations in learning rate, we compared the number of days required to

reach the predefined learning criterion (>70% correct and <30% incorrect choices across three consecutive training days). Our results showed no significant differences between *Fmr1*$^{-/y}$ mice and their WT littermates in the total number of training days to reach criterion (Fig. 1B) or in the duration spent at each stage of the training protocol (Fig. S1A-B, see Methods). Similarly, both genotypes required a comparable number of days to learn the association between stimulus salience and the correct lick-port (Fig. 1C-D). These results show that *Fmr1*$^{-/y}$ mice display an intact learning rate in this perceptual decision-making task.

Fmr1$^{-/y}$ mice display impaired performance on low-salience trials during perceptual learning.

Learning difficulties can manifest not only as slower task acquisition but also as reduced overall performance across the training period. To investigate this, we assessed the animals' sensitivity (d') in discriminating between high- and low-salience stimuli throughout training. *Fmr1*$^{-/y}$ mice showed a trend toward reduced overall task sensitivity compared to WT littermates (Fig. 1E), indicating diminished perceptual performance. Notably, this decreased performance was salience-specific: while *Fmr1*$^{-/y}$ mice performed comparably to WT mice during high-salience trials (Fig. 1F), they showed a strong trend toward reduced sensitivity for low-salience stimuli (Fig. 1G). These findings demonstrated that, despite acquiring the task at a comparable rate (Fig. 1B-D), *Fmr1*$^{-/y}$ mice exhibit selectively diminished perceptual performance under low-salience conditions.

Task performance reflects both correct and incorrect choices, which together determine the sensitivity index (d'). However, d' alone does not reveal how each component contributes to overall performance. To identify the source of reduced sensitivity in *Fmr1*$^{-/y}$ mice during low-salience trials (Fig. 1G), we separately analyzed correct and incorrect choice rates across the training period. Our results showed comparable correct choice rates in *Fmr1*$^{-/y}$ and WT mice (Fig. 1H), for both high- and low-salience stimuli (Fig. S1C-D). In contrast, *Fmr1*$^{-/y}$ mice presented a significantly higher rate of incorrect choices (Fig. 1I). This difference was specific to low-salience stimuli (Fig. 1J), while error rates for high-salience trials were comparable between genotypes (Fig. 1K). These findings demonstrate that reduced task performance in *Fmr1*$^{-/y}$ mice during low-salience trials is primarily driven by increased error rates, rather than a diminished ability to produce correct responses.

Salience-specific impaired performance is driven by higher choice consistency bias in _Fmr1_$^{-/y}$ mice.

The elevated error rates for low-salience stimuli in *Fmr1*$^{-/y}$ may reflect alterations in response bias (criterion) or expectation bias (*priors*). To assess whether an increased response bias—specifically, a tendency to repeatedly select the same lickport—contributed to this pattern, we evaluated the animal's overall decision strategy by calculating the decision criterion. This analysis revealed no significant differences in the decision criterion between *Fmr1*$^{-/y}$ mice and their WT littermates, indicating that both groups displayed no particular preference for one of the lickports (Fig. 2A).

Decisions are influenced not only by the sensory features of stimuli but also by the animal's previous experiences, which shape its expectations (i.e., *priors*). To investigate the impact of prior experience on current choices, we analyzed behavioral responses on a trial-by-trial basis. We first examined how a rewarded choice in the previous trial influenced the performance in the current trial (Fig. 2B). *Fmr1*$^{-/y}$ mice exhibited an increased rate of incorrect responses to low-salience stimuli when these were preceded by a rewarded high-salience stimulus (Fig. 2C). In contrast, no genotype difference was observed when a high-salience stimulus followed a rewarded low-salience trial (Fig. 2D).

We next tested whether *Fmr1*$^{-/y}$ mice were more influenced by their prior choices. To assess this, we compared the rates of repeated prior choices in current low- and high-salience trials, controlling for the total number of correct and incorrect responses. Our analysis revealed an increased impact of prior choices during low-salience trials in *Fmr1*$^{-/y}$ compared to WT mice (Fig. 2E), but a comparable impact of prior choices during high-salience trials (Fig. 2F).

To determine whether the observed difference in performance between WT and *Fmr1*$^{-/y}$ mice was due to their reliance on priors, rather than an inherent difference in the priors themselves, we assessed the strength of the priors created by high- and low-salience stimuli. Specifically, we calculated the rate of choices that were repeated following a low- or high-salience trial, correcting for the overall rate of correct and incorrect responses. Our results showed similar prior strength between groups, both for high-salience (Fig. S2A) and for low-salience stimuli (Fig. S2B).

Taken together, these findings demonstrate that a stronger choice consistency bias during low-salience trials results in the increased number of incorrect choices during these trials in *Fmr1*$^{-/y}$ mice, reducing their task performance during perceptual learning.

Fmr1$^{-/y}$ mice do not show attention deficits during perceptual learning.

Stimulus salience is closely linked to attentional processes (Kerzel and Schönhammer, 2013; Forschack et al., 2022; Bouvier et al., 2023), and attentional alterations are well-documented in autistic individuals (Allen and Courchesne, 2001; Grubb et al., 2013; Barbot et al., 2018; Licznerski et al., 2020; Rong et al., 2021b). Given that *Fmr1*$^{-/y}$ mice exhibit salience-dependent performance differences during training (Fig. 1-2), we asked whether their reduced task performance might also reflect underlying attention deficits. To assess attention, we analyzed the trials in which the animal failed to respond to the stimulus (Miss trials) (Fig 1A). Within-genotype analysis confirmed studies linking salience and attention in humans (Kerzel and Schönhammer, 2013), revealing significantly higher Miss rates for low-salience trials in both groups (Fig. S2E). However, there were no genotype differences in Miss rates for either high- or low-salience stimuli (Fig. S2C-D). These data demonstrate that low-salience stimuli are less effective in capturing attention in both *Fmr1*$^{-/y}$ and WT mice and that the decreased task performance in *Fmr1*$^{-/y}$ mice cannot be attributed to an attentional deficit during low-salience trials.

Trained _Fmr1_$^{-/y}$ mice show enhanced discrimination of low-salience stimuli.

Altered tactile discrimination has been reported in clinical studies (reviewed in (Zetler et al., 2019)) and in mouse models of autism (Orefice et al., 2016; Balasco et al., 2021, 2022; Mattioni et al., 2024). To assess tactile discrimination in our study, we incorporated the original training stimuli along with 6 intermediate amplitudes, spaced 2 µm apart. Stimuli ranging from 20 to 26 µm (20, 22, 24, 26 µm) were categorized and rewarded as high-salience stimuli, while those from 12 to 18 µm (12, 14, 16, 18 µm) were treated as low-salience stimuli (Fig. 3A). Only animals that successfully acquired the task during the training phase were included in the tactile discrimination test. *Fmr1*$^{-/y}$ and WT mice showed similar performance during the last three days of training, with no significant differences in task sensitivity (Fig. S3A-C), rates of correct (Fig. S3D-E) and incorrect responses (Fig. S3F-G), behavioral strategies (Fig. S3H), use of priors (Fig S3I-N), or attention (Fig. S3O-P).

To evaluate task performance, we quantified the rate of right-lick responses, corresponding to reports of high-salience stimuli. Psychometric curves were constructed based on these high-salience responses and showed no significant differences in the overall responses between the two groups (Fig. 3A).

We then assessed the animals' ability to discriminate high-salience stimuli by comparing the proportion of right-lick responses to 26 µm and 24 µm stimuli. Our results showed that neither WT nor *Fmr1*$^{-/y}$ mice were able to reliably distinguish between these two amplitudes (Fig. 3B). However, both groups reliably discriminated between 26 µm and 22 µm stimuli (Fig 3C). These results demonstrate that high-salience stimuli differing by 4 µm in amplitude can be discriminated by both genotypes.

We next investigated low-salience stimulus discrimination by comparing the rate of right-lick responses (reporting high salience) to stimuli of 12 µm and 14 µm amplitude. WT mice responded similarly to both stimuli (Figure 3D), consistent with their performance on high-salience stimuli differing by 2 µm (Fig. 3B). In contrast, *Fmr1*$^{-/y}$ mice exhibited enhanced discrimination accuracy for these low-salience stimuli, with increased high-salience report rates for the 14 µm stimuli compared to those for 12 µm (Fig. 3D). This enhanced discrimination accuracy in *Fmr1*$^{-/y}$ mice was further validated by comparing their low-salience reports. *Fmr1*$^{-/y}$ mice showed decreased low-salience lick rates for the 14 µm stimuli compared to the 12 µm, while WT mice exhibited comparable responses for both stimulus amplitudes (Fig. 3E).

Together, these results demonstrate that *Fmr1*$^{-/y}$ mice present enhanced tactile fine-discrimination for low-salience stimuli.

Fmr1$^{-/y}$ mice exhibit intact salience categorization.

In addition to assessing stimulus discrimination, our task allowed us to evaluate whether *Fmr1*$^{-/y}$ and WT mice form the same categories of low- and high-salience stimuli. Using the psychometric curves of the animals' high-salience responses (Fig. 3A), we measured the categorization threshold and accuracy. No differences were observed between *Fmr1*$^{-/y}$ mice and their WT littermates regarding their categorization threshold (Fig. 3F) or accuracy (slope, Fig. 3G), showing comparable salience categorization between groups. Overall task sensitivity (d'; Fig. 3H) as well as sensitivity on high- or low-salience trials were also similar between genotypes (Fig. S4A-B). Furthermore, *Fmr1*$^{-/y}$ mice showed similar rates of correct (Fig. S4C-D) and incorrect choices (Fig. S4E-F) compared to their WT littermates. In conclusion, these results demonstrate similar categorization of high- and low-salience stimuli in *Fmr1*$^{-/y}$ and WT mice.

Fmr1$^{-/y}$ mice show decreased impact of categorization on stimulus discrimination.

According to the Adaptive Resonance Theory, categorization recruits both bottom-up sensory processing and top-down cognitive control mechanisms. Top-down feedback upon categorization can amplify perceptual differences between stimuli belonging to different categories and reduce perceived differences within a category (Goldstone, 1994). Alterations in this top-down feedback have been reported in autistic individuals, who, despite showing similar categorization of visual stimuli (in line with our findings, Fig. 3F–G), exhibited a reduced influence of categorization on perceptual discrimination (Soulières et al., 2007). To examine whether salience categorization differentially impacts tactile discrimination in WT and *Fmr1*$^{-/y}$ mice, we compared the discrimination accuracy for stimulus pairs that differ by 2 µm and either span across different salience categories (across-category, i.e., 18 µm and 20 µm stimuli) or fall within the same category. Discrimination accuracy was calculated as the difference in rightward choices between each pair of stimuli.

Our results showed a reduced influence of categorization on perceptual discrimination in *Fmr1*$^{-/y}$ mice, which depended on the salience of the stimuli. In WT mice, the discrimination accuracy for across-category stimulus pairs was consistently higher than for within-category low-salience pairs (Fig. 4A-C), reflecting a fourfold increase in accuracy (Fig. 4G). In contrast, *Fmr1*$^{-/y}$ mice did not show this facilitative effect of categorization on perceptual discrimination, exhibiting similar across-category and within-low-salience discrimination accuracy for the majority of the low-salience pairs (Fig. 4A-C). This led to a strong trend toward reduced facilitation of across-category discrimination in *Fmr1*$^{-/y}$ mice (Fig. 4G). In contrast, for high-salience stimuli, both WT and *Fmr1*$^{-/y}$ mice showed enhanced discrimination for the across-category pair compared to within-category discrimination, suggesting preserved categorization effects under high-salience conditions (Fig. 4D–F, 4H).

Taken together, these findings demonstrate a reduced facilitation of across-category discrimination by categorization in *Fmr1*$^{-/y}$ mice, particularly when compared to their performance on within-category low-salience discriminations.

Reduced top-down categorization influence improves low-salience stimulus discrimination in *Fmr1*$^{-/y}$ mice.

Categorization not only facilitates the discrimination of stimuli belonging to different categories but also reduces the discrimination of stimuli belonging to the same category. A reduced top-down feedback of categorization on low-salience stimuli might thus explain the enhanced discrimination of these stimuli in *Fmr1*$^{-/y}$ mice (Fig. 3G). To investigate this hypothesis, we assessed the influence of categorization on within-category discrimination by comparing the discrimination accuracy for the stimuli furthest apart within the low- or high-salience categories. Increased discrimination accuracy in this case indicates a smaller influence of categorization on within-category discrimination. Our results showed a trend for increased discrimination accuracy within the low-salience category in *Fmr1*$^{-/y}$ mice (Fig. 4I) while no differences were observed between the groups for discrimination within the high-salience category (Fig. 4J). This result was further confirmed by comparing the average discrimination accuracy for each pair of low-salience stimuli, which was higher in *Fmr1*$^{-/y}$ mice compared to WT animals (Fig. 4K). Taken together, these data demonstrate decreased overall impact of categorization on low-salience stimuli that may facilitate the discrimination of these stimuli in *Fmr1*$^{-/y}$ mice (Fig. 3D), thus accounting for their enhanced low-salience discrimination.

Response bias and impact of priors during tactile categorization and discrimination are intact in *Fmr1*$^{-/y}$ mice.

During perceptual category learning, *Fmr1*$^{-/y}$ mice exhibited intact response bias but elevated choice consistency bias for low-salience trials (Fig. 2A, C, E). To determine whether similar alterations might also affect tactile discrimination performance and potentially contribute to the enhanced low-salience discrimination observed in *Fmr1*$^{-/y}$ mice, we analyzed both response strategy and the influence of prior choices during the discrimination phase.

To evaluate response strategies of the animals during tactile discrimination, we assessed their decision criterion, derived from the sensitivity index (d') across high- and low-salience stimuli. No difference in overall strategy was observed between *Fmr1*$^{-/y}$ mice and their WT littermates (Fig. S5A), as both groups showed no systematic preference for either lick port. We also found a similar impact of priors during tactile discrimination in both genotypes, with comparable effects of previous choices in high- and low-

salience trials (Fig. S4B–E). Together, these findings show that neither response bias nor the influence of priors accounted for the enhanced low-salience discrimination observed in *Fmr1*$^{-/y}$ mice. Furthermore, the strategy and priors of trained mice (Fig. S3I-L) remained stable during tactile discrimination and categorization.

High-cognitive load conditions lead to salience-dependent attention deficits in *Fmr1*$^{-/y}$ mice.

According to the Load Theory of Selective Attention, the extent of cognitive load modulates the attentional capacity (Lavie and Dalton, 2014; Murphy et al., 2016). During the tactile discrimination/categorization phase of our task, animals were subjected to a high cognitive load, as they had to categorize and discriminate among eight stimulus intensities to obtain a water reward. Leveraging this design, we examined whether *Fmr1*$^{-/y}$ mice display attentional deficits by assessing the rate of miss trials as a proxy for attention.

While no difference was observed in the miss trial rate for high-salience stimuli between genotypes (Fig. 5A), *Fmr1*$^{-/y}$ mice exhibited a strong trend toward decreased attention to low-salience stimuli, resulting in an increased miss trial rate (Fig. 5B). This attention deficit was specific for the stimulus of lowest salience (12 µm, Fig. 5C) and was not observed for low-salience stimuli of higher amplitudes (Fig. 5D-F). Strikingly, this attention deficit was not observed during the training period, when only one high- and one low-salience stimulus is presented, and the cognitive load of the task is lower (Fig. S2B, Fig. S3N). Taken together, these results demonstrate a salience-specific attention deficit in *Fmr1*$^{-/y}$ mice under high cognitive load conditions, despite their enhanced discrimination of these stimuli.

Discussion

Here, we developed a decision-making task based on psychophysics to dissociate stimulus-driven from cognitively-modulated tactile responses in the *Fmr1*$^{-/y}$ mouse model of autism. Our findings reveal salience-dependent cognitive alterations that shape sensory performance. During perceptual learning, *Fmr1*$^{-/y}$ mice exhibited cognitive alterations, characterized by an increased choice consistency bias during low-salience trials, which contributed to reduced task performance. Following training, *Fmr1*$^{-/y}$ mice displayed an enhanced tactile sensitivity under low-salience conditions—driven by decreased influence of the higher-order cognitive process of categorization. Although cognitive processes modulated sensory responses, attentional impairments under high cognitive load were independent of the enhanced tactile sensitivity in *Fmr1*$^{-/y}$ mice. Our findings highlight the interplay between sensory and cognitive alterations in autism, emphasizing the importance of cognitive context in interpreting sensory phenotypes, and advocating for a shift beyond traditional sensory–cognitive dichotomies to better understand autism-related phenotypes.

Learning alterations in autism and reliance on priors

Learning disability and intellectual disability are the second and third most common co-occurring neurodivergencies of autism, observed in 23.5% and 21.7% of autistic individuals, respectively (Khachadourian et al., 2023). Notably, even in the absence of these co-occurring conditions, autistic individuals exhibit differences in learning processes and altered neural mechanisms of learning (Mercado et al., 2020). In our study, we observed reduced performance in salience-based perceptual learning, driven by a high consistency bias in choice selection in *Fmr1*$^{-/y}$ mice. These results align with findings in autistic individuals showing a stronger influence of previous choices on current perceptual decisions (Feigin et al., 2021). Moreover, decreased flexibility in perceptual decision-making is consistent with evidence of

altered auditory and visual learning in autism (Harris et al., 2015; Alispahic et al., 2022), decreased performance under volatile conditions (Goris et al., 2021), as well as increased perseveration and diminished sensitivity to feedback (Crawley et al., 2020). Perceptual category learning was also found to be slower in autistic individuals, potentially due to the use of strategies that prioritize response guessing over rule application (Bott et al., 2006; Soulières et al., 2011). Impairments in visual, tactile, and audio-visual perceptual learning have also been shown in *Fmr1*$^{-/y}$ mice (Arnett et al., 2014b; Goel et al., 2018; Mol et al., 2024). Our findings extend this body of work by identifying a salience-dependent shift in reliance on priors in autism, with lower-salience stimuli more strongly evoking dependence on previous choices and impacting perceptual learning.

Increased sensory discrimination in autism and top-down influence of categorization

Several theories of autism, including the *weak coherence* (Frith, 2003), *enhanced perceptual functioning* (Mottron et al., 2006), and *reduced generalization theories* (Plaisted, 2001), support the notion of a superior perception of low-level information in autism. Indeed, a body of work has confirmed superior pure tone discrimination (Bonnel et al., 2003; O'Riordan and Passetti, 2006) and discrimination learning of highly confusable patterns (Plaisted et al., 1998b).

Tactile discrimination in autism has been studied using diverse experimental protocols that target different tactile features, which has often led to contradictory results due to methodological variability and participant heterogeneity (reviewed in (Zetler et al., 2019)). Similarly, work on roughness discrimination in rodent models (Orefice et al., 2016; Ahmadi et al., 2023) and human studies (O'Riordan and Passetti, 2006) has shown discrepancies. To address translational challenges between animal models and clinical research, our approach employed vibrotactile stimuli closely aligned with those used in human studies. Consistent with findings in autistic individuals (He et al., 2021b), *Fmr1*$^{-/y}$ mice showed intact amplitude discrimination for high-salience vibrotactile stimuli. Importantly, our study further uncovered enhanced discrimination of low-salience stimuli in *Fmr1*$^{-/y}$ mice, an aspect that remains underexplored in autistic individuals. Clinical studies have typically employed stimuli with more than 10-fold higher amplitudes compared to stimulus detection thresholds (He et al., 2021b; Asaridou et al., 2022). In contrast, our investigation focused on suprathreshold stimuli with much lower intensities (1.5-fold higher above threshold amplitude, 4-fold higher frequency). Future clinical studies assessing the discrimination of lower-level stimuli are necessary to explore whether enhanced low-salience discrimination also characterizes autistic individuals, and to investigate the impact of categorization in the process.

Most perceptual discrimination is influenced by categorization (Goldstone, 1994; Beauny et al., 2020; Micher et al., 2024). The reduced generalization hypothesis of autism postulates that, apart from superior performance on a difficult discrimination task, autistic individuals will have inferior performance in stimulus categorization (Plaisted, 2001). However, studies on rule-based and prototype categorization have yielded inconclusive results, reporting both intact (Klinger and Dawson, 2001; Molesworth et al., 2005), slower (Soulières et al., 2011), reduced (Froehlich et al., 2012; Gastgeb and Strauss, 2012) and enhanced performance (Bonnel et al., 2003) in categorization tasks in autistic individuals.

We assessed for the first time the impact of top-down categorization processes on discrimination of vibrotactile stimuli in a mouse model of autism. Our results revealed that increased tactile discrimination in autism is directly linked to the decreased influence of categorization. Although no clinical studies to date have examined this question in the tactile domain, our findings are consistent with previous research in the visual modality. These studies suggest that enhanced discrimination in autistic individuals may stem from reduced generalization (Plaisted et al., 1998b; Plaisted, 2001), and further indicate that

discrimination processes may operate with increased independence from the top-down influences of categorization (Soulières et al., 2007). These findings suggest a bidirectional interaction between sensory and cognitive alterations in autism, indicating that not only atypical sensory perception can impact cognition (Haigh, 2018), but also that cognitive differences can, in turn, shape sensory processing.

The weak coherence theory of autism posits that individuals with autism exhibit heightened precision in processing details at the expense of integrating contextual information. Increased "local" processing could account for enhanced discrimination performance. However, in our study, *Fmr1*$^{-/y}$ mice exhibited enhanced discrimination only under specific stimulus salience conditions, arguing against a global increase in sensory processing precision. Furthermore, our results reveal that categorization selectively influences discrimination performance based on stimulus salience, pointing toward a top-down modulation of perception rather than enhanced bottom-up processing. Finally, the improved discrimination of low-amplitude stimuli in *Fmr1*$^{-/y}$ mice does not appear to result from increased attentional allocation to these stimuli, as this would predict decreased miss rates for these stimuli, which we did not observe.

Attentional alterations in autism

Although attention deficits are not considered a general characteristic of autism (Grubb et al., 2013), reduced attention in the presence of salient distractors (Venker et al., 2021) and weaker accuracy in executive attention (Ridderinkhof et al., 2018) have been reported in autistic individuals. While a body of work has demonstrated alterations in selective attention and distractor filtering during high cognitive load (Head and Helton, 2014; Lavie and Dalton, 2014; Brockhoff et al., 2022), less is known about attention to task-relevant stimuli. Our results support the view that attention deficits emerge under conditions of high cognitive load. Specifically, cognitive load appears to disproportionately affect attention to low-salience stimuli in *Fmr1*$^{-/y}$ mice, suggesting a disruption in late-stage attention processes, which take place after the stimulus is perceived and are involved in top-down goal-directed behavior (Calvillo and Jackson, 2014). In contrast, high-salience stimuli, which tend to capture attention automatically (Smallwood, 2013), may engage early attentional processes that are independent of late-stage attention and thus less affected by cognitive load. This context-dependent attentional modulation aligns with previous findings in autistic individuals, showing stimulus-dependent auditory attention deficits (Čeponiene et al., 2003). These findings suggest that attentional alterations in autism may be conditionally expressed, particularly under tasks requiring increased cognitive resources.

Our results further dissociate attentional and tactile alterations in *Fmr1*$^{-/y}$ mice, with low-salience stimuli being better discriminated but less attended to in *Fmr1*$^{-/y}$ mice. These findings indicate that attentional deficits are independent of sensory processing, reflecting studies on linguistic stimuli in autistic children (Järvinen-Pasley et al., 2008; Ploog, 2010).

While the strong correlation between tactile experience and other core symptoms of autism has been well-documented, it was shown that these alterations do not correlate with symptoms of co-occuring neurodivergencies like ADHD (He et al., 2021b), even though the attention deficits are very common in autistic individuals (Rong et al., 2021b).

Conclusion

Numerous hypotheses have sought to provide a unified explanation for the diverse symptoms of autism. Our findings support the notion that altered cognitive processes shape perception in autism, revealing

that reduced top-down modulation of sensory responses may underlie the distinct ways in which autistic individuals learn and engage with their environment. Future research is needed to determine whether these alterations arise from autonomous changes within top-down circuits or their feedback interactions with sensory systems, ultimately reshaping sensory representations. Elucidating how cognition affects sensory perception could offer valuable insights for clinical practice, enabling the development of more targeted and effective behavioral interventions.

Materials and Methods

Experimental design

To study tactile perception as well as attention and perceptual biases in autism, we developed a novel 2-Alternative Choice task for the categorization and discrimination of flutter-range vibrotactile stimuli. Throughout the text, we use terms that are preferred in the autistic community and are less stigmatizing (Bottema-Beutel et al., 2021).

Ethical statement

All experimental procedures were performed in accordance with the EU directive 2010/63/EU and French law following procedures approved by the Bordeaux Ethics Committee and Ministry for Higher Education and Research. Mice were maintained in reversed light cycle under controlled conditions (temperature 22–24 °C, humidity 40–60%, 12 h/12 h light/dark cycle, light on at 21:00) in a conventional animal facility with *ad libitum* access to food and *ad libitum* access to water before the water restriction period. All experiments were performed during the dark cycle, under red light.

Mice

Second-generation *Fmr1* knockout (*Fmr1*$^{-/y}$) and wild-type littermate mice 5-16 weeks old were used in our study. Mice were maintained in a C57Bl/6 J background (Mientjes et al., 2006). Male wild-type and *Fmr1*$^{-/y}$ littermates were generated by crossing *Fmr1*$^{+/-}$ females with *Fmr1*$^{+/y}$ male mice from the same production, and the resulting progeny used for our experiments was either *Fmr1*$^{+/y}$ (wild type) or *Fmr1*$^{-/y}$ (KO). Mice were maintained in collective cages following weaning (2-4 litter males per cage). Cages were balanced for genotype and supplemented with cotton nestlets and carton tubes. Number of mice are given in the figure captions. The genotype of experimental animals was re-confirmed post hoc by tail-PCR.

2-Alternative Choice task

Setup

The vibrotactile decision-making setup was positioned in an isolation cubicle to minimize interference during the experiment. Mice were placed in a body tube and were head-fixed with their forepaws resting on two steel bars (6 mm diameter, Thorlabs). The right bar was mounted to a Preloaded Piezo Actuator (P-841.6, Physik Instrumente) equipped with a strain gauge feedback sensor and controlled (E-501, Physik Instrumente) in a closed loop, as described before (Prsa et al., 2019). Water reward was delivered through either of the two metal feeding needles (20G, 1,9mm tip, Agntho's AB), placed left and right of the mouse's mouth, each connected to a lickport interface with a solenoid valve (Sanworks) equipped with a capacitive sensor (https://github.com/poulet-lab/Bpod_CapacitivePortInterface). The behavioral setup was controlled by Bpod (Sanworks) through scripts in Python (PyBpod, https://pybpod.readthedocs.io/en/latest/).

Habituation to head-fixation and water restriction

Mice (P40-P50) were handled using carton tubes and the cupping technique until they were comfortable in the experimenter's hands, attested by eating while handled. Mice were gradually habituated to the experimental setup and head fixation for 5 days. The third day of habituation, a water-restriction protocol was implemented, where mice had access to liquid water in the setup and to a solid water supplement (Hydrogel, BioServices) in their home cage. In total, the animals received 1.5-2 ml of water per day, which corresponds to 50-65% of their ad libitum consumption, while ensuring that they did not lose more than 10% of their weight. Each mouse received 6-8 g of Hydrogel (*ad libitum*) during the weekend. This water restriction protocol was maintained throughout behavioral training and until the end of behavioral testing.

2-Alternative Choice task training and testing

Habituated mice (8 weeks old) were trained to associate high- (26 µm) and low-salience (12 µm) vibrotactile stimuli (pure sinusoid, 500 ms duration, 40 Hz frequency) with a water reward (8 µl) at the right- or left-placed lickport of the setup, respectively. All trials consisted of stimulus delivery followed by a 2 s response window during which the mice could lick to receive the reward. Inter-trial intervals were variable (5-10 s). Training was subdivided in 4 phases: (a) automatic water delivery at the beginning of the response window at the corresponding lickport (left for 12 µm stimuli, right for 26 µm stimuli). (b) Training in blocks: lick-triggered water delivery during blocks of 20 trials with the same vibrotactile stimulus, of either 12 µm or 26 µm amplitude. Licking at the wrong port resulted in 5 s timeout. (c) Training with pseudorandomly delivered high- and low-salience trials: lick-triggered water delivery following pseudorandom delivery of 12 µm or 26 µm amplitude stimuli. Licking at the wrong port resulted in 5 s timeout.

All sessions consisted of 200-300 trials with a 1:1 ratio of high and low-salience stimuli. During training, this ratio was modified when an animal showed consistent bias for one of the two lickports. Pilot experiments with an extra sensor to monitor forepaw placement confirmed that the mice did not remove their forepaws from the bar before stimulus delivery. To complete training in blocks, mice needed to perform with 70% correct choices and 30% incorrect choices for both stimulus amplitudes. To complete training with pseudorandomly delivered high- and low-salience trials, mice needed to reach the criterion of more than 70% correct choices and less than 30% incorrect choices as an average for 3 consecutive days. All mice that fulfilled this criterion were tested for the categorization/discrimination of vibrotactile stimuli. During testing, stimuli (pure sinusoid, 500 ms duration, 40 Hz frequency) were delivered in a pseudorandom manner with a 50% High-salience: 50% Low-salience ratio. Amplitudes varied on a range between 12 µm and 26 µm. Stimuli of 20, 22, 24 and 26 µm were considered high-salience stimuli and rewarded at the right lickport while stimuli of 12, 14, 16 and 18 µm were considered as low-salience stimuli and rewarded at the left lickport.

2-Alternative choice vibrotactile task analysis

All analysis was performed with custom-made Python scripts. Behavior was quantified based on the lick events and three main outcomes were measured for each stimulus salience: Correct choice rate (number of correct licks divided by the total number of high- or low-salience trials), Incorrect choice rate (number of wrong licks divided by the total number of high- or low-salience trials), and Missed stimuli rate (number of trials in which the animal did not lick, divided by the total number of high- or low-salience trials). Training duration was calculated based on the total number of days each animal passed in training in blocks and with pseudorandom stimulus delivery. For testing, only sessions with more than 70% correct choices for the training stimuli (12 µm and 26 µm) were analyzed. Psychometric curves were fitted on the

rightwards lick rate for each stimulus amplitude using a general linear model. An average of 84 repetitions for each amplitude was used to calculate rightwards lick rates.

Categorization thresholds were calculated based on the psychometric curves, as the stimulus amplitude at the inflection point of the sigmoid fitting curve. Categorization accuracy was calculated based on the slope of the psychometric curve.

Based on the signal detection theory (Detection Theory,(Hautus, M.J., Macmillan, N.A., & Creelman, 2021)), sensitivity d' was calculated as:

$$d' = \frac{1}{\sqrt{2}} z(\text{Correct choice rate}) - z(\text{Incorrect choice rate})$$

Sensitivity d' for high- and low-salience stimuli was calculated based on the Correct and Incorrect choice rate for high- and low-salience stimuli respectively.

The strategy of the animals was assessed through their criterion, which was calculated as:

$$c = d'(\text{high}) - d'(\text{low}).$$

Prior choice impact was calculated separately for each type of the current trial (high- or low-salience). For low-salience trials the prior choice impact was calculated as the rate of correct low and incorrect-low trials, divided by the rate of all correct and all incorrect trials. Similarly, for high-salience trials the prior choice impact was calculated as the rate of correct high and incorrect-high trials, divided by the rate of all correct and all incorrect trials.

Statistics

All values are presented as mean ± s.e.m. Box plots show the median, interquartile, range, mean and individual values. The numbers of animals used are indicated in the figure legends. All statistical analysis was done using Python (SciPy, Pingouin). All datasets were tested for normality. Two-tailed unpaired or paired *t*-tests were performed to evaluate the difference between two groups of data. When normal distribution was not confirmed, the Mann-Whitney U test was used for comparisons between different groups, and the Wilcoxon Signed Rank test was used for within-group comparisons. Genotype effects in the constructed psychometric curves were tested with mixed linear model regression.

Figures and Figure Legends

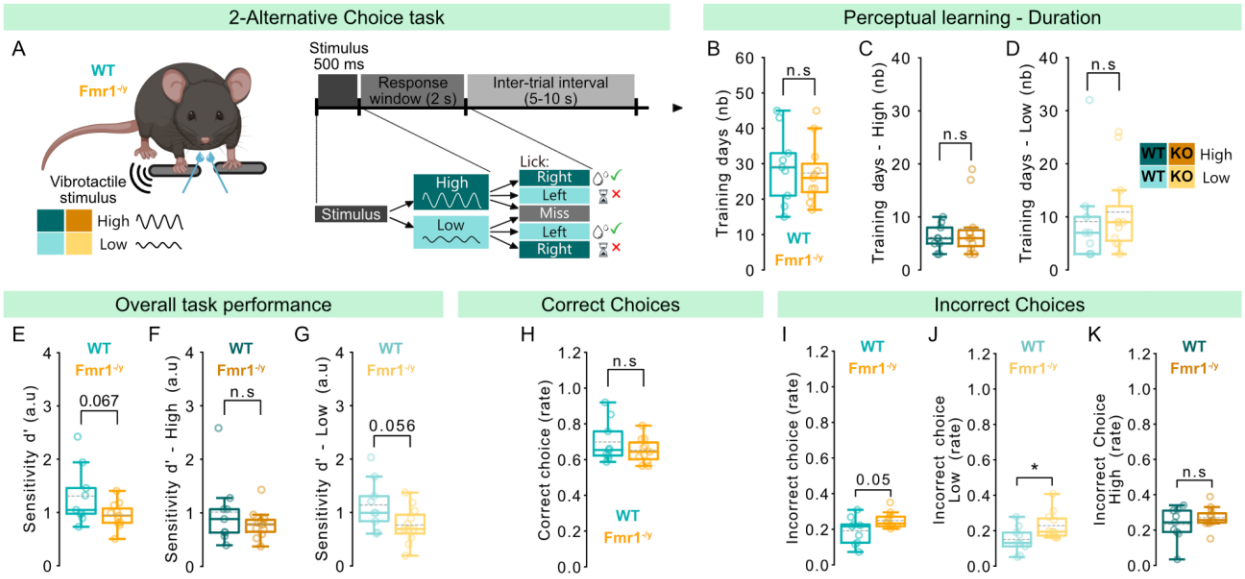

Figure 1. Perceptual learning performance in a forepaw-based decision-making task. For panels **B, C, D, E, F, G, H, I, J, K:** n=9 WT, 11 *Fmr1*$^{-/y}$ mice. **A,** Left: schema showing the behavioral setup. Right: Trail protocol and behavioral outcomes depending on the type of trial and the animal's response. **B,** Total number of days spent in training for WT and *Fmr1*$^{-/y}$ mice. **C,** Total number of days spent in training until the criterion was met for high-salience stimuli for WT and *Fmr1*$^{-/y}$ mice. **D,** Total number of days spent in training until the criterion was met for low-salience stimuli for WT and *Fmr1*$^{-/y}$ mice. **E,** Sensitivity d' throughout the training period for WT and *Fmr1*$^{-/y}$ mice. **F,** Sensitivity d' throughout the training period during high-salience trials for WT and *Fmr1*$^{-/y}$ mice. **G**, Sensitivity d' throughout the training period during low-salience trials for WT and *Fmr1*$^{-/y}$ mice. **H,** Correct choice rate for both high- and low-salience trails throughout the training period for WT and *Fmr1*$^{-/y}$ mice. **I,** Incorrect choice rate for both high- and low-salience trails throughout the training period for WT and *Fmr1*$^{-/y}$ mice. **J,** Incorrect choice rate for high-salience trails throughout the training period for WT and *Fmr1*$^{-/y}$ mice. **K,** Incorrect choice rate for low-salience trails throughout the training period for WT and *Fmr1*$^{-/y}$ mice. P values were computed using two-sided t-test for panels **B, E, G, H, I, J** ; Mann-Whitney test for panels **C, D, F, K** ; *P < 0.05 or n.s, not significant.

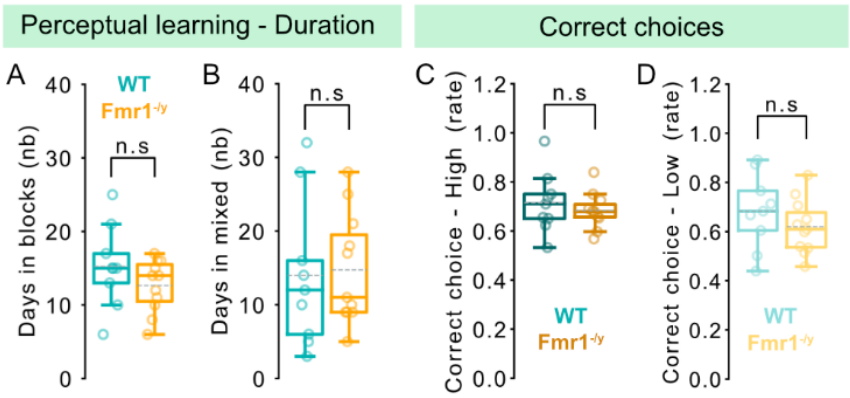

Figure S1. Perceptual learning duration for the different training phases and correct choice rates. n=9 WT, 11 *Fmr1*$^{-/y}$ mice. **A,** Total number of days spent in the training phase where stimulus delivery is done in blocks of high- or low-salience stimuli. **B,** Total number of days spent in training with high- and low-salience stimuli are delivered in a pseudorandom manner. **C,** Correct choice rate for high- salience trails throughout the training period for WT and *Fmr1*$^{-/y}$ mice. **D,** Correct choice rate for low- salience trails throughout the training period for WT and *Fmr1*$^{-/y}$ mice. P values were computed using two-sided t-test for panels **A, B, C, D** ; n.s, not significant.

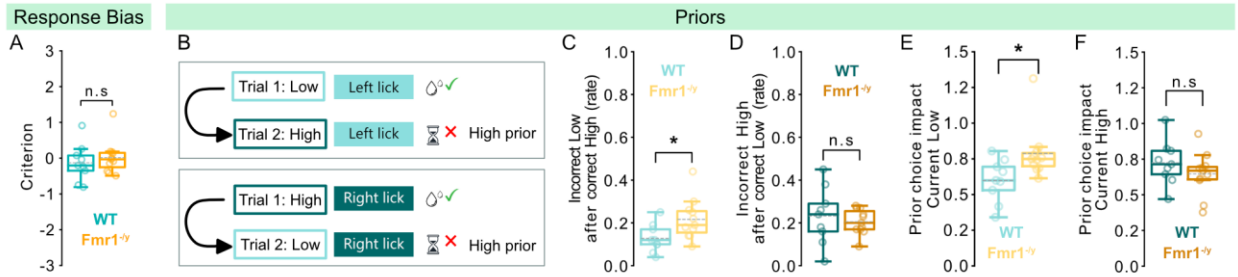

Figure 2. Overall strategy and impact of prior choice during perceptual learning. For panels **A, C, D, E, F:** n=9 WT, 11 *Fmr1*$^{-/y}$ mice. **A,** Criterion depicting the licking strategy of the animals. **B,** Schema showing an example of how high impact of prior choice on the current trial affects the response during a high-salience trial (top) or low-salience trial (bottom). **C,** Proportion of incorrect responses in low-salience trials immediately following a correctly rewarded high-salience trial. **D,** Proportion of incorrect responses in high-salience trials immediately following a correctly rewarded low-salience trial. **E,** Proportion of correct responses in low-salience trials immediately following a correctly rewarded low-salience trial and incorrect responses in low-salience trials immediately following a correctly rewarded high-salience trial. Rates are corrected over the total number of correct and incorrect choices in low-salience trials. **F,** Proportion of correct responses in high-salience trials immediately following a correctly rewarded high-salience trial and incorrect responses in high-salience trials immediately following a correctly rewarded low-salience trial. Rates are corrected over the total number of correct and incorrect choices in high-salience trials. P values were computed using two-sided t-test for panels **C, D, F,** ; Mann-Whitney test for panels **A, E,** ; *P < 0.05 or n.s, not significant.

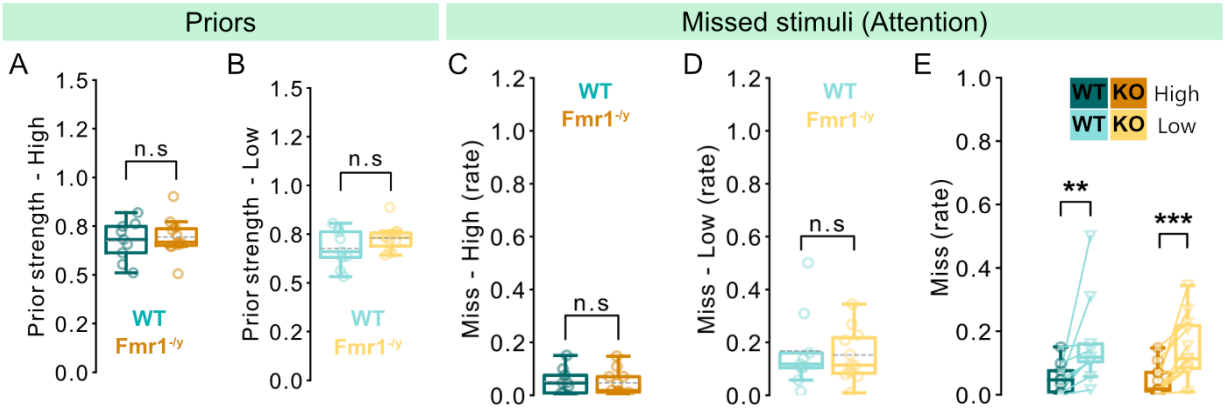

Figure S2. Prior strength and attention during perceptual learning. n=9 WT, 11 *Fmr1*$^{-/y}$ mice. **A,** Strength of the prior build for high-salience trials, calculated as the proportion of correct high-salience and incorrect low-salience responses following a correct high-salience response. Rates are corrected over the rate of overall correct high-salience and incorrect low-salience responses. **B,** Strength of the prior build for low-salience trials, calculated as the proportion of correct low-salience and incorrect high-salience responses following a correct low-salience response. Rates are corrected over the rate of overall correct low-salience and incorrect high-salience responses. **C,** Proportion of missed high-salience trials. **D,** Proportion of missed low-salience trials. **E,** Within-genotype comparisons of the proportion of missed high- and low-salience trials. P values were computed using two-sided t-test for panels **A, B,** ; Mann-Whitney test for panels **C, D,** ; Wilcoxon signed-rank test for panel **E**, ; ***P < 0.001, **P < 0.01, or n.s, not significant.

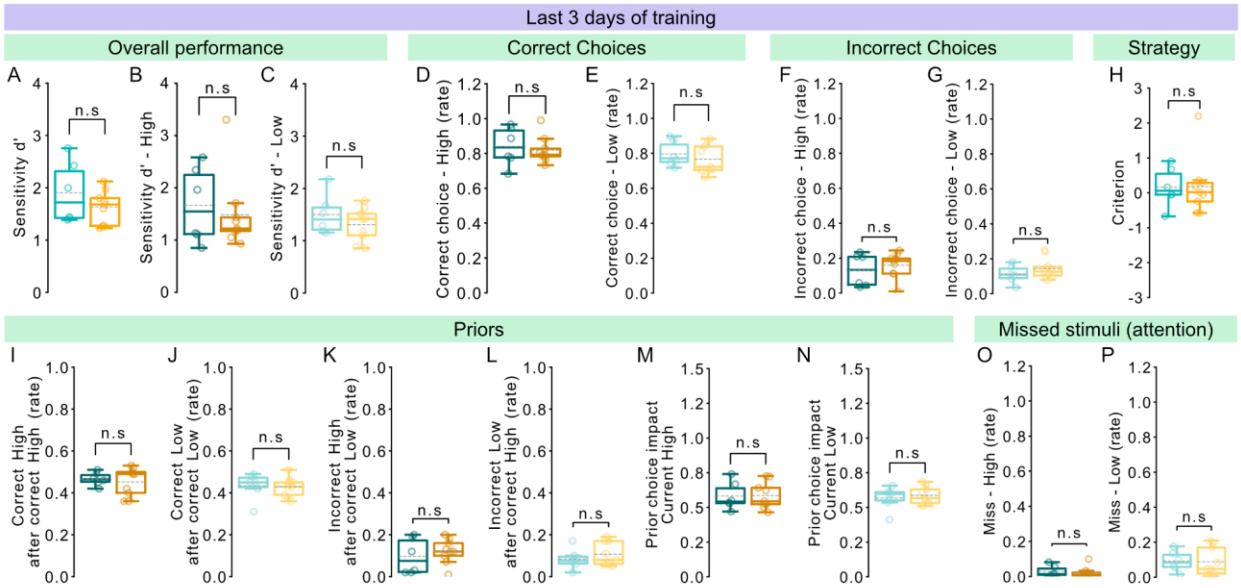

Figure S3. Perceptual learning performance during the last three days of training, for mice that were tested in tactile discrimination. n=6 WT, 9 *Fmr1*$^{-/y}$ mice. **A,** Sensitivity d' for both high- and low-salience trials throughout the last three days of the training period for WT and *Fmr1*$^{-/y}$ mice. **B,** Sensitivity d' for high-salience trials throughout the last three days of the training period. **C,** Sensitivity d' for low-salience trials throughout the last three days of the training period. **D,** Proportion of correct choices for high-salience trails throughout the last three days of the training period. **E,** Proportion of correct choices for low-salience trails throughout the last three days of the training period. **F,** Proportion of incorrect choices for high-salience trails throughout the last three days of the training period. **G**, Proportion of correct choices for low-salience trails throughout the last three days of the training period. **H,** Criterion depicting the licking strategy of the animals. **I,** Proportion of correct responses in high-salience trials immediately following a correctly rewarded high-salience trial. **J,** Proportion of correct responses in low-salience trials immediately following a correctly rewarded low-salience trial. **K,** Proportion of incorrect responses in high-salience trials immediately following a correctly rewarded low-salience trial. **L,** Proportion of incorrect responses in low-salience trials immediately following a correctly rewarded high-salience trial. **M,** Proportion of correct responses in high-salience trials immediately following a correctly rewarded high-salience trial and incorrect responses in high-salience trials immediately following a correctly rewarded low-salience trial. Rates are corrected over the total number of correct and incorrect choices in high-salience trials. **N,** Proportion of correct responses in low-salience trials immediately following a correctly rewarded low-salience trial and incorrect responses in low-salience trials immediately following a correctly rewarded high-salience trial. Rates are corrected over the total number of correct and incorrect choices in low-salience trials. **O,** Proportion of missed high-salience trials. **P,** Proportion of missed low-salience trials. P values were computed using two-sided t-test for panels **A, C, D, E, F, G, I, J, K, L, M, N, P** ; Mann-Whitney test for panel **O**; n.s, not significant.

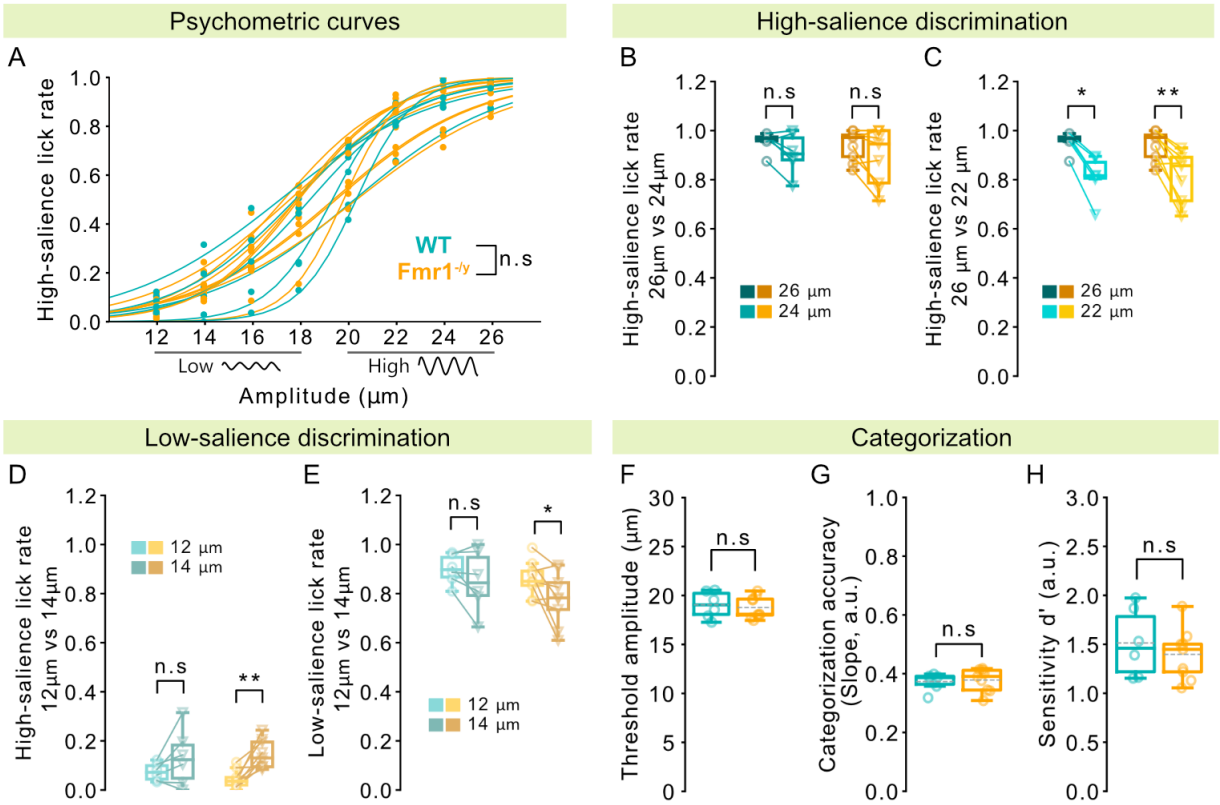

Figure 3. Tactile discrimination and categorization. n=6 WT, 9 *Fmr1*$^{-/y}$ mice. **A,** Psychometric curves for WT and *Fmr1*$^{-/y}$ mice generated based on the high-salience lick rate (rate of rightward licks) across 8 different amplitudes. Stimuli between 12–18 µm were designated as low-salience and rewarded at the left lickport, while stimuli between 20–26 µm were designated as high-salience and rewarded at the right lickport. Each amplitude was presented an average of 84 times. **B,** Comparison of high-salience (rightwards) responses for high-salience stimuli of 26 and 26 µm. **C,** Comparison of high-salience (rightwards) responses for high-salience stimuli of 26 and 22 µm. **D,** Comparison of high-salience (rightwards) responses for low-salience stimuli of 12 and 14 µm. **E,** Comparison of low-salience (leftwards) responses for low-salience stimuli of 12 and 14 µm. **F,** Categorization thresholds calculated based on the psychometric curves. **G**, Categorization accuracy computed based on the slope of the psychometric curves. **H,** Sensitivity d' of the responses in all stimulus amplitudes. P values were computed using Mixed Linear Model Regression (main effect of genotype) for panel **A,**; two-sided paired t-test for panels **B, C, D, E,;** two-sided t-test for panels **F, G, H,**; Wilcoxon signed-rank test for panels **B, C,;** **P < 0.01, *P < 0.05, or n.s, not significant.

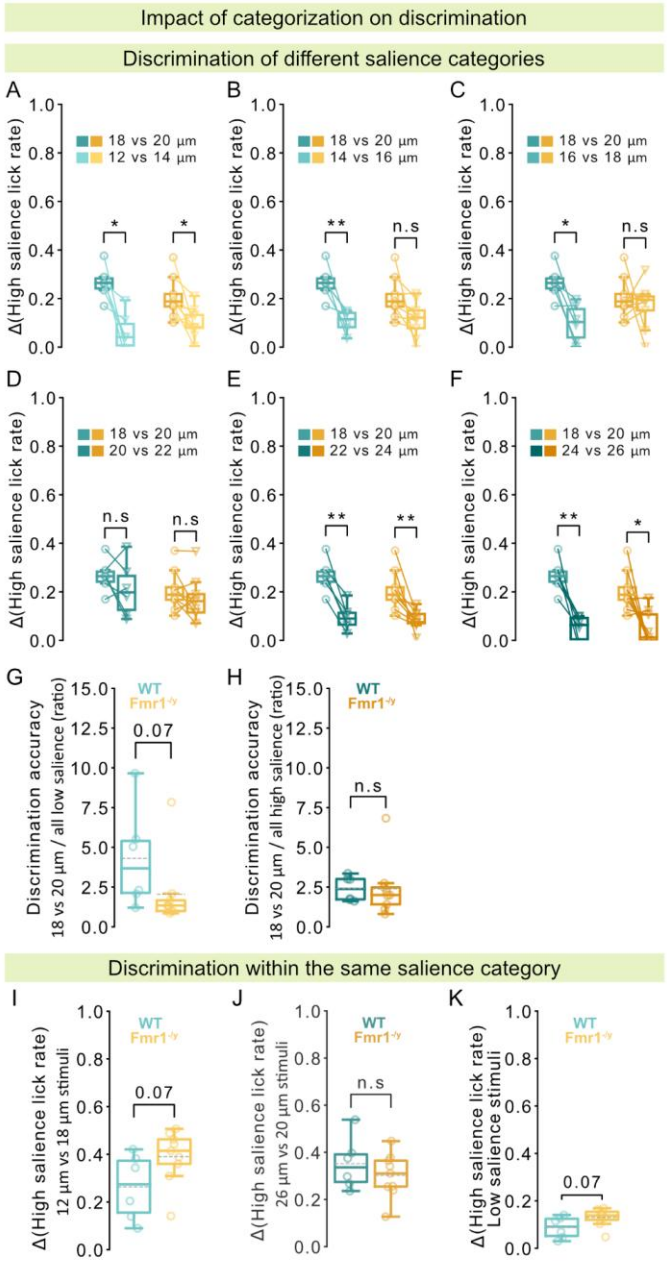

Figure 4. Impact of categorization on across-categories and within-category discrimination. n=6 WT, 9 *Fmr1*$^{-/y}$ mice. **(A-C)** Delta discrimination accuracy, calculated as the difference in the rate of high-salience licks between across-category stimuli (18 µm vs 20 µm) and within-category low-salience stimulus pairs: **A,** 12 µm vs 14 µm; **B,** 14 µm vs 16 µm; **C,** 16 µm vs 18 µm. **(D-F)** Delta discrimination accuracy, calculated as the difference in the rate of high-salience licks between across-category stimuli (18 µm vs 20 µm) and within-category high-salience stimulus pairs **D,** 20 µm vs 22 µm; **E,** 22 µm vs 24 µm; **F,** 24 µm vs 26 µm. **G,** Delta discrimination accuracy calculated as the difference in the rate of high-salience licks between the across-category stimulus pair (18 µm vs 20 µm) and the average discrimination across **G,** all low-salience stimulus pairs (12–14 µm, 14–16 µm, and 16–18 µm) and **H,** all high-salience stimulus pairs (12–14 µm, 14–16 µm, and 16–18 µm). **I,** Delta discrimination accuracy calculated as the difference in the rate of high-salience licks between the two extreme amplitudes within the low-salience category. **J,** Delta discrimination accuracy calculated as the difference in the rate of high-salience licks between the two extreme amplitudes within the high-salience category. **K,** Delta discrimination accuracy calculated as the difference in the rate of high-salience licks between all stimuli within the low-salience category. P values were computed using two-sided paired t-test for panels **A, B, C, D, E, F,;** Mann-Whitney test for panels **G, H,**; two-sided paired t-test for panels **I**, **J**, **K**,**;** **P < 0.01, *P < 0.05, or n.s, not significant.

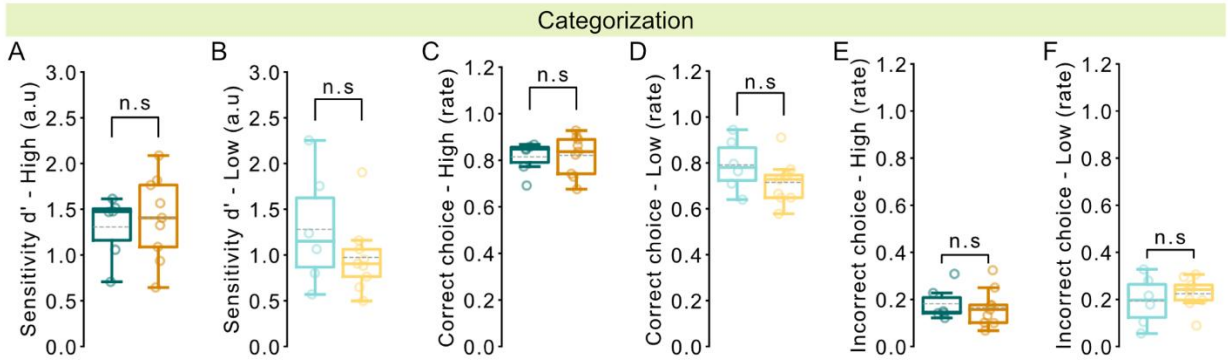

Figure S4. Sensitivity, correct, and incorrect choices during categorization of high- and low-salience stimuli. n=6 WT, 9 *Fmr1*$^{-/y}$ mice. **A,** Sensitivity d' for high-salience stimuli during categorization. **B,** Sensitivity d' for low-salience stimuli during categorization. **C,** Correct responses for high-salience stimuli during categorization. **D,** Correct responses for low-salience stimuli during categorization. **E,** Incorrect responses for high-salience stimuli during categorization. **F,** Incorrect responses for low-salience stimuli during categorization. P values were computed using two-sided t-test for all panels; n.s. not significant.

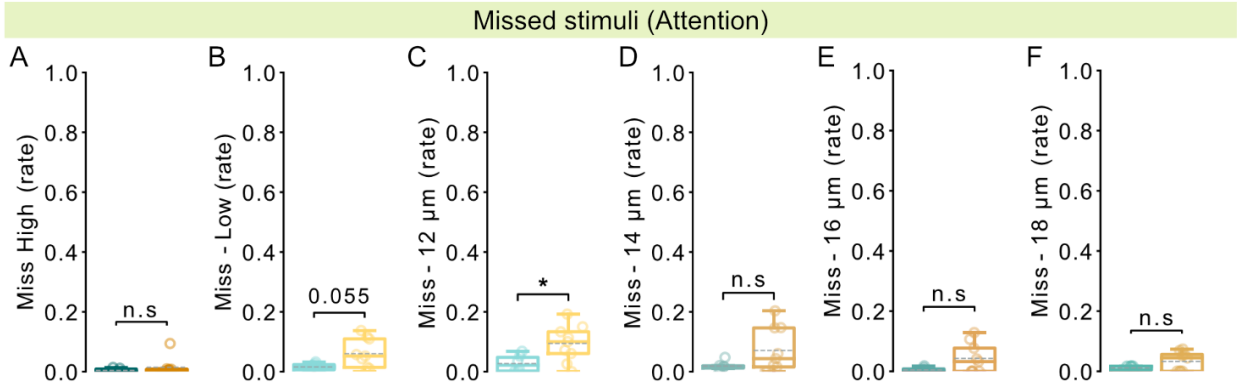

Figure 5. Attention in perceptual decision-making under high cognitive load. n=6 WT, 9 *Fmr1*$^{-/y}$ mice. **A,** Proportion of missed high-salience trials. **B**, Proportion of missed low-salience trials. **C,** Proportion of missed 12 µm low-salience trials. **D,** Proportion of missed 14 µm low-salience trials. **E,** Proportion of missed 16 µm low-salience trials. **F,** Proportion of missed 18 µm low-salience trials. P values were computed using Mann-Whitney test for panel **A, E, F**,; two-sided t-test for panel **B, C, D**,; *P < 0.05, or n.s, not significant.

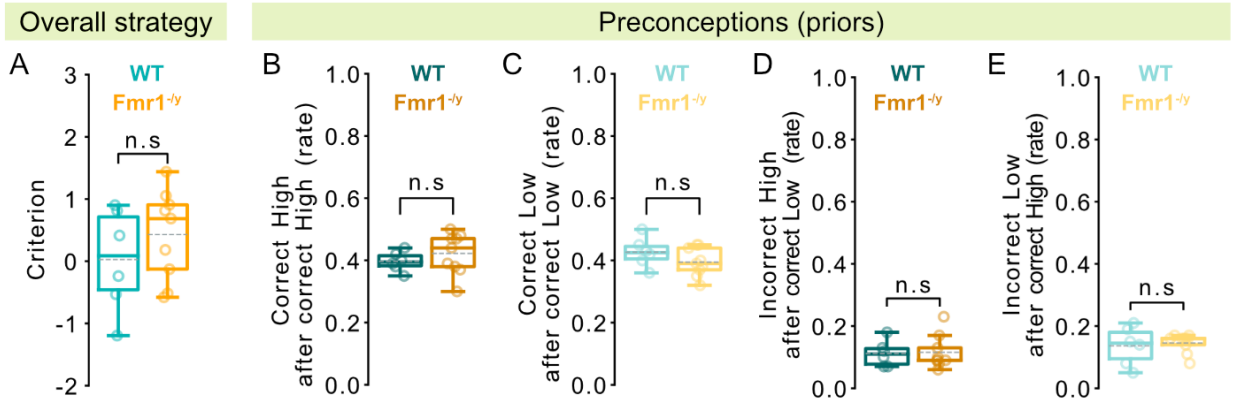

Figure S5. Overall strategy and impact of prior choice during stimulus categorization and discrimination. n=6 WT, 9 *Fmr1*$^{-/y}$ mice. **A,** Criterion depicting the licking strategy of the animals **B**, Proportion of correct responses in high-salience trials immediately following a correctly rewarded high-salience trial. **C,** Proportion of correct responses in low-salience trials immediately following a correctly rewarded low-salience trial. **D,** Proportion of incorrect responses in high-salience trials immediately following a correctly rewarded low-salience trial. **E,** Proportion of incorrect responses in low-salience trials immediately following a correctly rewarded high-salience trial. P values were computed using two-sided t-test for all panel **A, B, C, D**,; Mann-Whitney test for panel **E**,; n.s, not significant.

Acknowledgments
We would like to thank the animal housing and genotyping facilities of INSERM U1215 Neurocenter Magendie. We would like to thank Dr. Melanie Ginger for providing feedback on the manuscript. Mouse schemas were made using Biorender. This project was funded by the Foundation for Medical Research Postdoc Fellowship (O.S.), INSERM (A.F.), Marcel Dassault-Fondation FondaMental Award 2019 (A.F.), Simons Foundation Autism Research Initiative (A.F.), GIS Autisme & TND (O.S.), Fondation FondaMental.

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Contributions
A.F. and O.S. conceived the project. O.S. designed the experiments. O.S., M.T-M.F. and A.W. performed the experiments. O.S. and A.W. wrote the Python code for the behavioral experiments. O.S. analyzed the data and wrote the necessary Python scripts. O.S. interpreted the data. O.S. prepared the figures. O.S. wrote the manuscript, and A.F. and M.T-M.F. provided feedback.

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Ethics declarations
Competing interests
The authors declare no competing interests.

Inclusion and diversity statement
We support inclusive, diverse, and equitable conduct of research. We tried to use inclusive language as much as possible.

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