Sensory perception in autism

Caroline E. Robertson[1,2,3] and Simon Baron-Cohen[4]*

Abstract | Autism is a complex neurodevelopmental condition, and little is known about its neurobiology. Much of autism research has focused on the social, communication and cognitive difficulties associated with the condition. However, the recent revision of the diagnostic criteria for autism has brought another key domain of autistic experience into focus: sensory processing. Here, we review the properties of sensory processing in autism and discuss recent computational and neurobiological insights arising from attention to these behaviours. We argue that sensory traits have important implications for the development of animal and computational models of the condition. Finally, we consider how difficulties in sensory processing may relate to the other domains of behaviour that characterize autism.

Cognitive empathy
The ability to understand and respond appropriately to others' mental states and emotions (unlike affective empathy, the ability to respond with an appropriate emotion to others' mental states or feelings).

[1]*Harvard Society of Fellows, Harvard University, Cambridge, Massachusetts, 02138, USA.*
[2]*McGovern Institute for Brain Research, Massachusetts Institute of Technology, Cambridge, Massachusetts, 02139, USA.*
[3]*Department of Psychological and Brain Sciences, Dartmouth College, Hanover, New Hampshire, 03755, USA.*
[4]*Autism Research Centre, Department of Psychiatry, Cambridge University, Cambridge, CB2 8AH, UK*
**Correspondence to C.E.R carolinerobertson@fas.harvard.edu*

doi:10.1038/nrn.2017.112
Published online 29 Sep 2017

The ability to reflect on our own and others' thoughts and emotions (that is, theory of mind) is a defining characteristic of human cognition. Children with autism spectrum conditions (ASCs; henceforth 'autism') show delays in the development of this capacity[1], with knock-on consequences for cognitive empathy[2] across the lifespan. Interestingly, these alterations in social cognition are accompanied by a very different perceptual experience of the world. Atypical sensory experience is estimated to occur in as many as 90% of autistic individuals[3,4] and to affect every sensory modality: taste[5], touch[6,7], audition[8], smell[9,10] and vision[11]. A central challenge of autism research is to identify the common thread that unites these various aspects of cognition and sensation. What neurobiological alterations might affect processes as disparate as social cognition and sensory perception?

This challenge is highlighted by the latest international diagnostic criteria for autism, which now include sensory sensitivities as a core diagnostic feature[12]. Although sensory symptoms were noted in early reports of the condition[13], they have historically been construed as secondary aspects of autistic cognition rather than as primary phenotypic markers (see Supplementary information S1 (box)). As well as having clinical implications for creating autism-friendly environments, understanding the importance of sensory differences in autism is crucial for neurobiological accounts of the condition. Because the neural computations underlying sensory processing are relatively well understood in typically developing individuals and are conserved between humans and other animals, studies of sensory behaviour have considerable potential for shedding light on autistic neurobiology[14]. Further, as precursors to developmental milestones in social cognition, sensory symptoms could potentially serve as early diagnostic markers.

However, the issue of primacy is key. Is autism, as often posited, a disorder of the 'social brain' (REF. 15), with sensory differences representing either secondary consequences after a lifetime of reduced social interaction or alterations in domain-general mechanisms (such as attention) that affect both social processing and sensory processing? Or are the sensory differences primary in terms of both development and neurobiology?

Here, we explore whether sensory traits are, in fact, core phenotypic markers of autism. To do this, we apply four tests of core phenotypic status, by asking whether autistic sensory traits are present in early development, substantially improve diagnostic accuracy when included in diagnostic assessments, reflect alterations to neural circuitry in sensory-dedicated regions of the brain, and are evident in genetic animal models of the condition.

The evidence we review suggests that the autistic cortex is affected by distinct, low-level changes in neural circuitry that is dedicated to perceptual processing (including primary sensory areas). Further, perceptual symptoms in individuals with autism are evident early in development, account for independent variance in diagnostic criteria of the condition, and show a persistent relationship to clinical measures of higher-order social cognition and behaviour. We suggest that an understanding of the perceptual symptoms in autism may provide insight into signature differences in canonical neural circuitry that might underpin multiple levels of autistic features, and may thus help to elucidate autistic neurobiology. We also discuss how primary sensory changes might relate to higher-order aspects of cognition in autism.

Sensory processing in autism

Sensory symptoms have been clinically documented as early as 6 months of age in infants later diagnosed with autism[16,17] — considerably earlier than children reach key

developmental milestones in social cognition, such as joint attention (14–18 months)[18]. Sensory symptoms not only precede[17] but also are predictive of social-communication deficits[19] and repetitive behaviours in childhood[20], as well as eventual diagnostic status[19]. Assessments of sensory traits in the broader autism phenotype suggest a genetic component to these symptoms: the parents and siblings of individuals with autism show higher levels of self-reported sensory traits relative to the general population[21,22]. Importantly, greater atypicalities in sensory processing are observed in families that are thought to have higher genetic liability for autism (multiplex families) than in families with a single individual diagnosed with autism (simplex families), in which the genetic basis of autism is likely to be *de novo*[21].

Taken together, these findings suggest that such traits represent early markers of autism. Yet, are these traits primary, or do they simply reflect secondary outcomes of alterations in domain-general neural mechanisms, such as attention? In this section, we briefly review laboratory-based characterizations of autistic sensory behaviour, drawing particular attention to replicated findings in the literature (for in-depth reviews, see REFS 11,23–27), before approaching this question.

Visual detection

Individuals with autism have been characterized as 'seeing the trees, but not the forest': attuned to details of the perceptual world at the expense of the global percept they compose[28]. This framework for understanding autistic sensory experience emphasizes that perceptual processing cannot simply be characterized as a talent or a deficit[29] or as reflecting hypersensitivity or hyposensitivity. Rather, perceptual representation in autism exhibits a relative bias towards local over global features of a sensory scene, which can be more or less advantageous depending on task demands[30].

This detail-focused perceptual style is well captured by two studies of autistic visual behaviour (FIG. 1). First, individuals with autism often show faster detection of single details (targets) embedded in cluttered visual displays (that is, among distractors) and a relative insensitivity to the number of distractors in the display[31]. This visual search superiority in autism has been widely replicated[31–37] and extended as a promising early marker in toddlers through eye-tracking[38,39]. Second, machine-learning approaches have shown that gaze patterns from individuals with autism during passive viewing of naturalistic, complex scenes favour scene regions that rank high in pixel-level saliency (for example, regions that are salient in terms of contrast, colour or orientation) compared with object-level saliency (for example, relating to the size, density or contour complexity of objects) or semantic-level saliency (for example, of text, tools or faces), which drive gaze biases in neurotypical individuals[40]. This data-driven approach provides a compelling demonstration of detail-focused visual preferences in autism, even in the context of naturalistic viewing.

One prediction from these demonstrations would be that individuals with autism might have superior detection or discrimination thresholds for static stimuli[41]. However, perplexingly, basic measures of visual sensitivity such as visual acuity[37,42], contrast discrimination[43,44], orientation processing, crowding[45,46] and flicker detection[47,48] have all been shown to be typical in autism, leaving unresolved the question of how the autistic brain gives rise to rapid and accurate perception of detail. There are some replicated atypicalities in low-level visual processing in autism, particularly in the domain of high-spatial-frequency stimuli[49,50], but these are unlikely to account for the full magnitude of autistic superiority in visual search, where stimuli are not necessarily of high spatial frequency.

Temporal synthesis of sensory signals

If basic visual detection thresholds for static, local stimuli are typical in autism, why do individuals with autism display altered local–global processing? One possibility is that perceptual processing in autism may be marked not by an overall bias towards enhanced local perception but rather by a shift in the temporal pattern of local–global processing towards slower global processing[51]. This may particularly affect dynamic visual representations, which are by their nature built up over time. This hypothesis rests on evidence from research suggesting that temporal processing of local sensory signals is slower and/or noisier in individuals with autism in the domains of visual, tactile, auditory and multisensory processing.

Visual motion processing. Unlike with static stimuli, individuals with autism often exhibit atypical processing of dynamic (social or non-social) visual stimuli[52–54] (FIG. 1). Although detection thresholds for local motion are typical[55] or even superior in autism[56,57], individuals with autism often struggle with global motion perception: that is, the ability to discern the global direction (for example, rightward or leftward motion) of a 'cloud' of local visual motion signals (for instance, moving dots)[58,59]. These deficits are predictive of the severity of higher-order autistic symptoms[58,59] and are particularly pronounced when the motion signal is weak or the time to integrate is short[58,59], suggesting that global motion processing in autism is not disrupted *per se* but evolves more slowly over time.

Tactile perception. As in the visual domain, evidence for alterations in basic tactile detection thresholds in autism is mixed — with some studies finding typical[60,61] and others reporting superior[62] or reduced sensitivity compared with controls[7] — although the tactile paradigms used in these studies vary. One difference in autistic tactile perception is well replicated: whereas control individuals present worse detection thresholds for stimuli that gradually increase in amplitude over time into a detectable range (reflective of dynamic thresholds) relative to acute stimuli (which require static thresholds), dynamic presentation does not impair tactile sensitivity in individuals with autism[7,63]. This difference is proposed to stem from reduced feedforward inhibition in the autistic sensory cortex[7,64], consistent with magnetoencephalography findings[65], and again suggests alterations in the temporal features of sensory processing in autism.

Joint attention
An early-developing cornerstone of social cognition: the child's ability to use another person's gestures and gaze to direct his or her attention to objects or events in the environment.

Broader autism phenotype
Mild autistic traits (in both social and sensory processing domains) often observed in relatives of individuals with autism in multiplex families.

Multiplex families
Families in which multiple individuals have an autism diagnosis; family members may carry shared genetic risk factors.

Crowding
The breakdown of visual recognition of peripheral stimuli in cluttered visual environments.

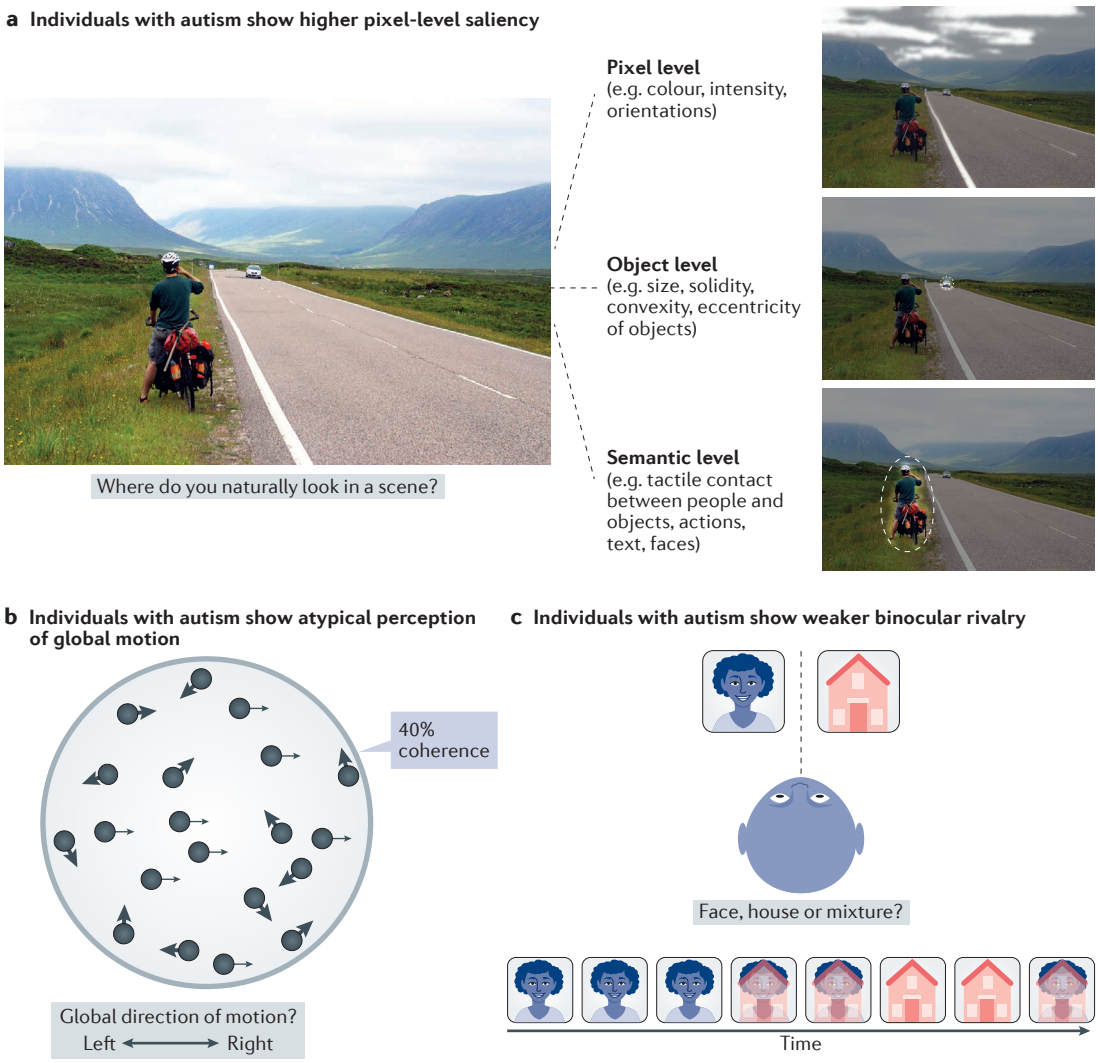

Figure 1 | **Trade-off in visual perception in autism. a** | In naturalistic viewing, gaze patterns of individuals with autism reveal greater preferences for scene regions with high pixel-level saliency (for example, regions of high contrast, colour or orientation) at the expense of regions rich in semantic-level saliency (for example, regions including tactile contact between people and objects, actions, text and faces)[40]. The photograph has been modified as an example to highlight these various levels of image features. **b** | In dynamic visual displays, individuals with autism require longer presentation times and higher signal-to-noise ratios to determine the general direction of dynamic stimuli (in the example, a set of dots moving generally to the right with 40% coherence)[53,59]. **c** | Individuals with autism show weaker binocular rivalry. Here, two images, one presented to each of an individual's eyes, alternate back and forth in perception as each is suppressed in turn by competitive interactions in visual cortex. In autism, individuals report (via button press) fewer perceptual switches between the inputs to their left and right eyes, as well as a reduced strength of perceptual suppression (when one image is fully suppressed from visual awareness). This replicated behavioural signature of autism in vision is predictive of the severity of social cognition symptoms measured using the Autism Diagnostic Observation Schedule (ADOS)[127,132,133].

Auditory perception. Similar disruptions in the temporal envelope of sensory processing have been observed in the domain of auditory processing in autism. Children with autism often show difficulty discerning the relative presentation order of two closely occurring tones[66] and show delayed evoked neural responses to auditory tones compared with typically developing children[67,68]. This latency in auditory responses predicts autism symptom severity[69] and is observed in response to pure tones as well as to complex, social stimuli (such as speech sounds)[70], raising the hypothesis that this difference might precipitate higher-order autistic difficulties in communication[71,72].

Multisensory binding. Converging evidence suggests a deficit in multisensory integration in autism, both in humans[69,70,73–78] and in animal models[76,79]. Specifically, individuals with autism demonstrate an elongated window of audio–visual temporal binding: relative to control individuals, they are less able to discern the presentation

order of a tone and flash at close temporal offsets and are more likely to perceive asynchronous events as synchronous[74,80]. Further, whereas control individuals are faster to detect a visual stimulus when presented with an auditory tone as opposed to when presented alone, this behavioural benefit is reduced in autism, paralleled by a reduction in multisensory facilitation measured using electroencephalography[81]. Deficits in multisensory binding are particularly observed with audiovisual speech paradigms[74,80,82,83] and may be developmental cornerstones of deficits in language and communication[84] (see below).

A temporal processing problem? In sum, altered temporal processing of sensory stimuli is seen in several sensory modalities in autism. Specifically, in autism, local stimuli often elicit delayed evoked responses in the auditory domain, and integration of multiple local stimuli into a global percept often requires a wider window of temporal binding. These differences may particularly tax multisensory processing, in which stimuli must be integrated from two sensory modalities[85], and dynamic perception, in which signals are built up over time.

Yet are these processing differences actually differences in sensation, or could they result from atypical modulation of sensory processing by higher-order cognitive mechanisms? For example, superiority during conjunctive search could arise from differences in parallel processing[86], deficits in judging global motion in two-alternative forced-choice tasks could arise from altered decision criteria[87], and reductions in multisensory binding could arise from differences in the cognitive mechanisms involved in drawing causal inferences[88]. In the next section, we discuss neuroimaging findings that demonstrate differences in the low-level primary sensory areas of the autistic brain.

Neuroimaging evidence

Consistent with the psychophysical evidence indicating a low-processing-level origin of the local–global perceptual style in autism, neuroimaging evidence strongly suggests that autistic sensory traits are indeed low-level in origin (FIG. 2). Atypical responses in primary sensory cortices have been observed in autism, across sensory modalities and during multimodal perception.

Global-motion perception tasks (FIG. 1b) involve both sensory and decision-making processes and have therefore been particularly useful in determining whether autistic perceptual differences are truly sensory in origin[89–91]. The slower integration of local motion signals into a global percept observed in autism[58,59,92,93] (discussed above) could be caused either by an atypical representation of local motion signals in early visual cortex (in the primary visual area (V1) and the primary motion area (MT)) or by alterations in the decision criteria by which these signals are integrated (in the intraparietal sulcus (IPS)) over time into a global percept[58]. Functional MRI (fMRI) studies have revealed that whereas the IPS response is typical in autism in these tasks, V1 and MT show reduced responses to low-strength motion signals (that is, with short durations and/or low coherence) in autism — presumably limiting the rate at which motion signals can be integrated into a global percept at higher-order processing stages[59]. Atypical V1 and MT responses in autism have been observed in several motion-processing studies[94–97], although whether they can account for deficits in perceiving biological motion in the condition, or simply contribute to differences in processing non-social global motion stimuli, is debated[98].

In further support of a low-level origin of autistic sensory differences, a robust signature of autistic sensory cortices is an increase in the inter-trial (within-individual) variability of evoked responses[99–101] (FIG. 2b). This replicated difference affects the visual, somatosensory and auditory cortices of individuals with autism (with some exceptions[102]) and differentiates people with autism from individuals with schizophrenia[103] (BOX 1). This finding may reflect a disruption of the excitatory–inhibitory balance (E–I balance), which typically modulates the trial-by-trial reliability of evoked sensory responses, in the autistic cortex[104]. Alterations in the functional architecture of sensory cortex have been observed as well: larger population receptive fields have been measured in extrastriate regions of the autistic visual cortex, including MT, and these co-vary with autistic traits[105] (FIG. 2b). Another persistent finding in neuroimaging studies of autism is unexpected cross-activation of visual cortex during auditory tasks[77] — potentially reflecting auditory–visual synaesthesia, which is more common in people with autism than in the general population[106].

Together, these findings indicate that neural signatures of autism are evident in early sensory processing — as early as in primary sensory regions of the autistic brain. Granted, attention modulates neural responses in these early sensory regions[107,108]; thus, it is difficult to attribute group differences in primary sensory areas to local changes in sensory signalling rather than to top-down attentional modulation, especially given that direct manipulations of attentional load are lacking in the fMRI studies described above. However, neuroanatomical changes in low-level primary sensory regions of the autistic brain suggest local alterations in the circuitry of sensory cortex. For example, cortical minicolumns are reported to be wider in both the primary auditory cortex and higher-order association areas in autism[109] (but see REF. 110). Moreover, behavioural studies suggest that atypical attentional deployment is unlikely to explain the detail-focused visual perception in autism: although people with autism show sharper enhancement of visual performance around a cued location than do control individuals[111,112] and have difficulties tracking multiple moving objects regardless of object speed[113], these individuals show typical measures of visual performance at the peak of a cued location[46,114].

Overall, this pattern of findings is compatible with the hypothesis that sensory differences are core phenotypic markers of autism. Higher-order neural processes that govern how sensory representations are modified by attention, integrated towards decision criteria, or influenced by task demands and expectation may also be altered in autism. However, given the evidence for alterations in primary sensory cortex during perceptual processing in autism, higher-order differences alone are unlikely to account for the perceptual experience of

Population receptive fields
A model-driven quantitative measurement of the average size and shape of receptive fields contained within a single functional MRI voxel.

Cross-activation
Activation of one sensory-dedicated cortical region by sensory stimulation of another modality.

Synaesthesia
The cross-activation of one sensory modality by stimulation of another.

Cortical minicolumns
Basic anatomical units of the neocortex, in which neurons are arranged in vertical columns across cortical layers of the brain.

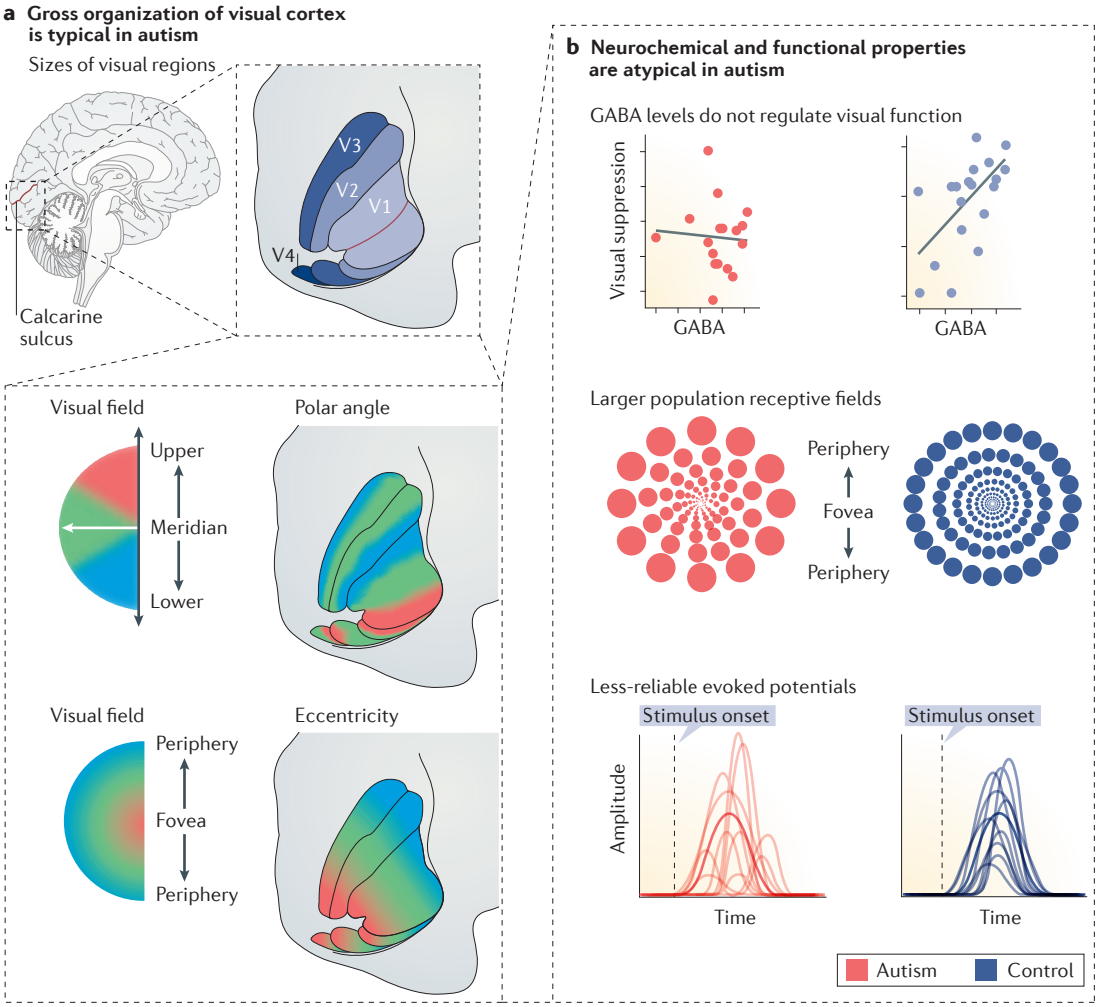

Figure 2 | **Neuroimaging evidence for low-level origin of visual symptoms in autism.** Atypical representations in primary sensory areas have been observed in autism in different sensory modalities. **a** | In the visual cortex, the gross organizational properties of visual areas are typical in terms of the surface area devoted to each early visual cortical region (V1, V2, V3 and V4); the cortical magnification function (that is, the ratio in the cortical area dedicated to foveal versus peripheral representations; not shown); and retinotopic maps, the cortical area dedicated to each part of the visual field, assessed in terms of polar angle (upper and lower visual fields) or eccentricity (distance from the fovea)[105]. **b** | However, distinct changes in the neurochemical composition, functional architecture and signalling fidelity of early visual cortex are observed in autism. Specifically, magnetic resonance spectroscopy (MRS) measurements implicate GABA in visual suppression deficits in autism[127]. Control individuals evidence a tight linkage between the strength of visual suppression and GABA levels in visual cortex, but this link is absent in autism (upper graphs). Measurements of the size of population receptive fields in the visual cortex find larger population receptive fields in autism[105] (shown schematically in the middle graphs). Cortical responses evoked by sensory stimuli (including moving dots, auditory tones and tactile stimuli), as measured using functional MRI, are less reliable in individuals with autism[100,103] (schematic responses shown here in the lower two graphs). The upper two graphs in part **b** are adapted with permission from REF. 127, Cell Press/Elsevier.

individuals with autism. With this in mind, we consider some putative alterations in low-level neural circuitry that may characterize sensory regions of the autistic brain.

Circuit-level insights

As the neural mechanisms of sensory perception have been well characterized using electrophysiology and psychophysical approaches, sensory symptoms may offer concrete insights into circuit-level differences in the autistic brain[14]. Indeed, our understanding of the neurobiology of autism has undergone many advances owing to tests of neural circuitry theories of the condition in the domain of sensory perception. Here, we focus in particular on the hypothesis that the autistic sensory cortex might be marked by differences in GABAergic signalling, as this hypothesis has been tested using neuroimaging approaches as well as computational approaches.

Reduced GABAergic signalling

E–I imbalance is posited to be a central characteristic of the neurobiology of autism, inspired in part by the high prevalence of seizures (perhaps as high as 1 in 3 by adolescence)

Binocular rivalry
A visual phenomenon in which two images, presented simultaneously to the two eyes, alternate in perception as neuronal pools coding for each eye's percept compete for perceptual dominance.

Spatial suppression
A visual phenomenon in which motion discrimination is counter-intuitively attenuated at larger, instead of smaller, stimulus sizes, probably owing to suppressive interactions (centre–surround antagonism or inhibitory feedback).

Critical period
A developmental period during which a neural system (such as vision) is particularly plastic and sensitive to environmental influence.

among people with autism[115]. GABA receptor perturbations have been associated with autism through genetic[116–121] and histological studies[122], and GABAergic signalling is disrupted in several different mouse models of autism[123,124]. The pivotal roles of GABA in canonical cortical computations[125] and neurodevelopment[126] indicate that the GABAergic signalling pathway is key to the neurobiology of autism[12].

Magnetic resonance spectroscopy (MRS) studies have linked disruptions in autistic visual processing[126,127] to GABA concentrations in early visual cortex (including V1). Specifically, binocular rivalry — a basic visual function that depends on the strength of inhibitory interactions in visual cortex[128–131] — is weaker in autism[127,132,133], and this deficit is associated with reduced GABAergic action in early visual cortex[127] (FIGS 1c,2b). This replicated behavioural signature of autism is also predictive of the severity of social cognition symptoms measured using the Autism Diagnostic Observation Schedule (ADOS)[127,132]. Two further MRS studies have reported reduced GABA levels in auditory and somatosensory cortex of autistic individuals[127,134], suggesting that reduced inhibition may characterize several cortical regions and perhaps underpin several sensory traits in autism.

Several behavioural and neuroimaging findings regarding autistic visual perception have been theoretically linked to altered inhibitory neurotransmission in the brain. Findings of decreased spatial suppression[134,135], atypical representations of motion signals[58,59], more within-individual variability in evoked responses[100,136] and expanded population receptive fields[105,137] each recapitulate the effects of blocking GABAergic sensory signalling in animal studies[104,138,139]. Yet, which part of the GABAergic pathway might be atypical in autism remains unclear. Mixed evidence implicates the availability of GABA itself[140], the prevalence or integrity of GABA receptors[141–144], the polarity of GABAergic action (which shifts from excitatory to inhibitory during the critical period of development)[145], and the density of cortical inhibitory interneurons[123].

Moreover, various other neurotransmitters and neuromodulators of GABAergic signalling may have a role in autistic sensory symptoms. For example, given that excitatory and inhibitory signalling typically exhibit homeostatic coupling during sensory development[146] and learning[147], alterations in GABAergic signalling in autism might be expected to be accompanied by alterations in excitatory signalling. Indeed, higher levels of glutamate in blood plasma[148] and higher glutamate

Box 1 | **Comparison with other psychiatric conditions**

Although much progress has been made in characterizing differences in sensory processing in autism, less is known about which of these differences are unique to autism or are seen in other neurodevelopmental conditions. This point is crucial for the early identification and translational potential of sensory behavioural assays. Survey-based studies have detected higher rates of sensory abnormalities in autism compared with other developmental disabilities, such as Down syndrome[219]. However, these questionnaire-based observations can only measure the magnitude of sensory sensitivities in a condition, rather than the characteristics of sensory processing. Below, we review key empirical findings that highlight similarities and differences in sensory function between autism and other psychiatric conditions. This evidence of patterns of sensory-processing differences in Rett syndrome, schizophrenia and dyslexia that are distinct from those in autism lends support to the notion that specific deficits in autistic sensory behaviour may indeed be able to serve as selective, objective markers of autism.

Rett syndrome

Until the recent revision of the *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition* (DSM-V)[12], Rett syndrome (RTT) was included under the diagnostic umbrella of the autism spectrum, as individuals with RTT have many phenotypic similarities to individuals on the autism spectrum. However, the sensory profile of individuals with RTT is distinct from that of individuals with autism. Notably, individuals with RTT exhibit differences to control individuals even in basic visual acuity paradigms[171,220], whereas similarly basic measures of low-level visual function (including visual acuity, contrast sensitivity and flicker detection) are typical in individuals with autism[42].

Schizophrenia

Given the evidence for genetic overlap between schizophrenia and autism[221], common sensory paradigms have been used to investigate these conditions. Importantly, such paradigms have revealed distinct patterns of sensory behaviour differences in autism and schizophrenia. For example, whereas neural responses evoked by sensory stimuli are more variable in autism[100], individuals with schizophrenia show typical response variance and lower-amplitude evoked responses[103]. Second, although reduced surround suppression is consistently observed in schizophrenia in many perceptual tasks[222–224], similar deficits are only seen in autism at low stimulus contrasts[134]. Last, whereas a robust reduction in perceptual suppression during binocular rivalry has been observed in autism[127,132,133], the opposite finding — increased perceptual suppression — is reported in schizophrenia[225]. Together, these findings illustrate distinct profiles of alterations in sensory processing in people with autism and individuals with schizophrenia.

Dyslexia

Individuals with dyslexia, similar to individuals with autism, often demonstrate deficits in global-motion perception compared with controls[226] and reduced activity in the primary motion area in neuroimaging studies[227]. However, evidence suggests that global-motion-processing deficits in dyslexia are secondary to reduced time spent reading, rather than being primary to the condition[228]: deficits are not observed when individuals with dyslexia are compared with reading-matched typical controls and are ameliorated by reading training[229].

Divisive normalization
A canonical neural computation in which the activity of a neuron is divided by the total activity of neighbouring neurons to reflect context-dependent responses.

Pre-pulse inhibition
A sensory phenomenon in which the behavioural response to a strong sensory stimulus is dampened by a weak preceding stimulus, probably through feedforward inhibition.

receptor expression[149] have been observed in individuals with autism, although empirical links with autistic symptoms have not yet been reported. Other neuromodulators, such as testosterone and oxytocin, modulate GABAergic signalling[150–152] and are associated with autistic traits[153–155]. Future research is needed to establish the role of these, and other, molecules in modulating inhibitory signalling in regions of the autistic brain.

Computational accounts

To date, most circuit-level computational accounts of autism build on a seminal theory that proposed an excitation-dominant imbalance of neurotransmission in the autistic brain[156]. On the basis of this theory, two computational models that attempted to recapitulate specific aspects of autistic sensory behaviour support the hypothesis of reduced inhibition relative to excitation in autistic visual circuitry[157,158].

In the first account, Vattikuti and Chow[157] demonstrate that an excitation-dominant circuit could simulate reports of less-precise saccadic targeting (dysmetria) and reduced saccadic velocity (hypometria)[159–162] in autism. The model predicts an increase in recurrent excitatory activity in the autistic cortex. In turn, this increase is predicted to reduce the spatial specificity of the neural population code for a saccadic target (leading to dysmetria) and to dampen sensitivity to activity from outside the self-excitatory system, therefore decreasing the rate at which saccadic switching between targets can occur (leading to hypometria). A second model[158] implicates reduced inhibition in a specific neural computation in autism. The authors propose that reducing the spatial spread of inhibition during divisive normalization may recapitulate two behavioural results in the autism literature: reduced spatial suppression[134] and sharper spatial processing[112] (but see REF. 14).

Computational approaches draw together disparate findings under a unifying framework that, when informed by circuitry-level models of neural function, may reveal generalizable principles of neural differences in autism. However, a key limitation of such approaches is that they are developed *post hoc* to recapitulate select behavioural deficits and thus risk losing explanatory and predictive power. We recommend that future computational studies of autistic behaviour be coupled with empirical tests of their predictions in novel experimental paradigms.

Overall, converging evidence from neuroimaging, psychophysics and computational modelling supports the long-held hypothesis that altered GABAergic inhibition may underpin visual symptoms in autism. Given the pivotal roles of GABA in canonical cortical computations[125] and neurodevelopment[126], future work will need to interrogate whether the neural changes to the circuitry in the visual system also characterize other regions of the autistic cortex.

Translational research

Two lines of research support the notion that investigations into sensory behaviours might provide promising translational tools for autism research (BOX 2; FIG. 3). First, *de novo* mutations associated with autism converge on pathways that influence synaptic connectivity, signalling and plasticity[163] and therefore would be predicted to affect wide-ranging neural processes such as sensory perception that are not necessarily confined to the 'social brain'. Second, increasing evidence suggests that sensory traits are present in common genetic models of autism. For example, mice with mutations in *Mecp2*, *Gabrb3*, *Shank3* or *Fmr1* (which encode methyl-CpG-binding protein 2, GABA type A receptor ($GABA_AR$) subunit-β3, SH3 and multiple ankyrin repeat domains protein 3, and fragile X mental retardation protein 1, respectively) all demonstrate tactile hypersensitivity, as measured in pre-pulse inhibition paradigms[124,164]. These sensory traits are specifically linked to the loss of $GABA_AR$-mediated inhibition in both *Mecp2*-mutant mice and *Gabrb3*-mutant mice[124], suggesting that disrupted GABAergic neurotransmission is a common feature in multiple genetic models of autism[123,124,165,166] (but see also REF. 167).

Genetic animal models of autism have also been shown to exhibit deficits in multisensory perception. Mice harbouring genetic mutations in *Gad2* (also known as *Gad65*; encoding glutamate decarboxylase 2), *Shank3* or *Mecp2* show reduced electrophysiological signatures of multisensory integration, which are again specifically linked to reduced GABAergic signalling in neural regions implicated in integrating cross-modal input

Box 2 | **Genetic animal models of autism**

Genetically modified animals represent a powerful tool for discovering circuit-level alterations in autistic neurobiology. The contribution of genetics to autism is well established: autism heritability is as high as 54–88% for monozygotic twins, compared with 10–33% for dizygotic twins[230,231], and many genetic risk factors for autism have been identified through copy number variant, genetic-linkage and genome-wide association studies[232,233]. Notably, gene variants that confer high penetrance for autism occur in a small subset of the autism population — fewer than 2% of individuals with the condition[234,235] — suggesting that the genetic aetiology of autism is complex and polygenic. Nevertheless, diverse genetic mutations may have converging downstream effects on specific biological pathways[236]. Thus, studying neural development in single-gene mutant animal models of autism may shed light on the aetiology of the condition by identifying common neurobiological pathways affected by different autism-associated mutations, along with their contributions to autistic-like traits in animals.

Animal models of human psychiatric conditions are typically held to three standards of validity: construct validity (whereby the condition is caused by the same biological alteration as in humans), face validity (the behaviour of the animal bears a strong resemblance to human behaviour), and predictive validity (the responses to therapy are likely to translate into humans)[237]. Genetic models of autism are exemplars of the first of these standards, construct validity, as they model a specific genetic mutation that is found in people with autism.

However, a major challenge for animal research is the lack of face and predictive validity. Behavioural symptoms in animals rarely present a compelling analogue to human experience, in part because most core features associated with autism in humans manifest in social cognitive functions, such as theory of mind or language comprehension, which are arguably human-specific. Behavioural assays in animal models of autism have traditionally focused on analogues for repetitive behaviours and social anxiety, such as marble burying and sociability[237] — traits that are not specifically related to autism but that also manifest in models of obsessive–compulsive disorder and social anxiety.

Translatable behavioural assays in autism research would facilitate the discovery of generalizable principles about neural circuitry that can move from animals to humans. Measures of sensory behaviour represent promising avenues for such translational assays, given the conserved nature of neural computations involved in sensory processing between animals and humans[14].

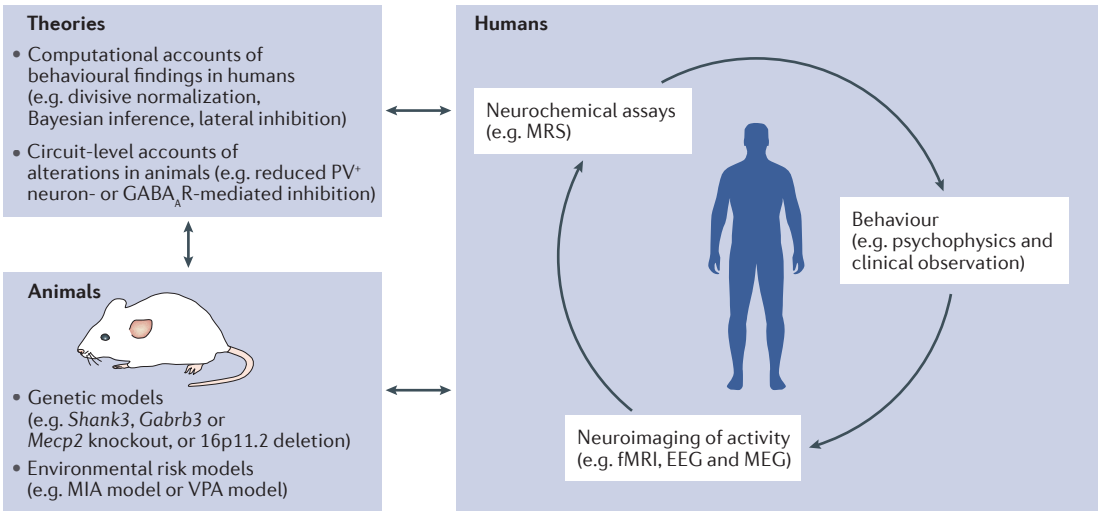

Figure 3 | **Sensory symptoms as translational behavioural markers of autism.** Given the well-characterized and evolutionarily conserved nature of sensory circuitry in the brain, perceptual symptoms represent a clear tool for translational research. Animal-level research can motivate the design of sensory paradigms in humans and, conversely,aid in delineating alterations in neural circuitry that produce behavioural traits in humans as well as downstream neural targets that merit investigation in humans. When animal-level research implicates a specific neurotransmitter pathway, human neuroimaging methods (magnetic resonance spectroscopy (MRS) or positron emission tomography (PET)) can probe the integrity of this pathway in humans and test whether it underpins behavioural differences. Computational and circuit-level theories of human and animal-level findings can help to uncover principles of neural function that might generalize across sensory paradigms, across sensory modalities and even to other domains of autistic traits. A crucial next step is to test whether genetic models of autism recapitulate the observed human-level behavioural differences using identical sensory paradigms. EEG, electroencephalography; fMRI, functional MRI; GABA$_A$R, GABA type A receptor; MIA, maternal immune activation; MEG, magnetoencephalography; PV$^+$, parvalbumin-expressing; VPA, valproic acid.

(including the insular cortex), and which can be rescued by pharmacologically enhancing GABAergic signalling in early development[76]. These atypical electrophysiological and behavioural markers of sensory processing across multiple monogenic models of autism independently implicate reduced GABAergic inhibition in the aetiology of these features.

Interestingly, one animal model study argues for a feedforward developmental role for sensory deficits in the broader autism phenotype. Specifically, targeted prenatal (but not adult) silencing of GABAergic inhibition in peripheral somatosensory neurons, sparing the CNS, produced tactile sensitivities and social interaction deficits in mice[124]. Importantly, this finding suggests that sensory symptoms in development alone may be sufficient to produce social deficits. Further work is needed to isolate the subcircuits by which this GABAergic deficit in somatosensory pathways led to these social-processing deficits, as well as the relevance of these findings to humans.

Despite these parallel findings in human and animal studies, a lack of directly comparable behavioural paradigms currently limits the potential of studies of sensory behaviour to serve translational research (BOX 2). One naive assumption in animal research is that sensory perception in autism can be ubiquitously characterized as 'hypersensitive' — a generalization that, as we have seen, does not capture the nuances of sensory behaviour in people with autism. Standard tests of 'hypersensitivity' used in the animal literature, such as startle response or pre-pulse inhibition, show mixed results in people with autism[168–170]. Thus, we suggest that a standardized set of sensory paradigms that demonstrate clear psychophysical differences in humans and that are suitable for translation into animals would enable validation of animal models of autism and further research into the neurobiology of the condition.

An elegant example of work that paves such a clear translational path can be found in the Rett syndrome (RTT) literature. Here, neural and behavioural sensory phenotypes established in animal and human models strongly correspond: *Mecp2*-knockout mice and individuals with RTT both exhibit a reduction in the amplitude of visually evoked responses in V1 and reduced spatial visual acuity[165,171]. Interestingly, in the case of the *Mecp2*-knockout mice, these differences stem from a reduction in the activity of GABAergic parvalbumin-expressing interneurons, which affects both excitatory and inhibitory responses[165]. Current candidate paradigms and measures for translational autism research may include binocular rivalry[127,132,133], multisensory perception[69,70,73–78] and latency of auditory responses[67,68] (FIG. 3).

Linking with higher-order traits

The co-occurrence of autistic differences in both low-level perceptual behaviour and high-level social-cognitive processing is a central puzzle of autism research. One clue

McGurk effect
A perceptual illusion in which a sound (for example, of the syllable /ba/) paired with a visual signal (a mouth pronouncing /ga/) produces a third percept (voice and mouth /da/).

Pragmatics
The ability to use the social context of an utterance to inform and communicate meaning.

is that perceptual differences in individuals with autism often predict the severity of higher-order autistic traits[36,38,52,69,105,112,127,172–177] in the laboratory setting. Large-scale studies also demonstrate covariance between questionnaire-based measures of sensory sensitivities and autistic traits in the general population[11,177,178], in both Western and Japanese cultures[179]. This correlation presents a strong argument for a relationship between sensory and social-cognitive processing in autism (BOX 3).

Neurobiological accounts of how and why these lower- and higher-order symptoms might be related in autism are largely divided into two camps. 'Sensory-first' accounts posit that social-cognitive symptoms may be downstream effects of atypical sensory processing in early development, whereas 'top-down' accounts posit that symptoms in sensation and social cognition might co-arise from alterations in domain-general mechanisms (such as attention, decision-making or causal inference) that affect both levels of information processing in the brain.

In this section, we discuss evidence for and against these accounts. There are, of course, many theories of autism that offer elegant accounts of one domain — but not multiple domains — of autistic features[11,41,180,181]; however, here we focus only on theories that offer a unifying account of diverse domains of autistic behaviour. Finally, we highlight a third approach, which we call the 'canonical micro-circuitry view', that posits that disparate levels of autistic features share common neural mechanisms.

Box 3 | **Time to give up on a unified account of autism?**

Some have argued that it is time to give up on a centralized account of autistic traits and that perhaps the disparate categories of autistic symptoms each have independent genetic causes and neural origins[238]. This argument largely rests on studies of autistic personality traits in large normative twin samples (including more than 3,000 twin pairs), which suggest that the degree of parent-reported autistic-like trait severity in social, communicative and repetitive behaviours are only modestly genetically related in typically developing children[239–241]. Further, autistic-like trait severity in typically developing children sometimes 'peaks' in single trait areas: it is estimated that 10% of children show autistic traits in only one symptom domain[238].

By contrast, studies of individuals with autism suggest stronger genetic overlap between autistic symptom domains. One small twin sample of autistic individuals found that common genetic factors represent the primary drivers of both social-communication symptoms and repetitive behaviours, with high heritability[242]. Furthermore, if autistic symptom domains are indeed fractionable, it remains perplexing that autistic perceptual symptoms often strongly co-vary with social-cognitive symptoms both at the population level[175–178,214] and in the laboratory[36,38,52,105,112,127,172–174], as well as with clinical assessments of repetitive behaviours[20,243,244].

Resolving the question of whether autistic behavioural domains are indeed fractionable will require overcoming three limitations of past studies. First, strong phenotypic measures of autistic behaviour across symptom domains that can be adapted for large-scale studies are needed to directly probe the relationship between symptom domains, rather than relying on measures of parental report, which show only modest test–retest reliability[240]. Second, genotyping individuals with autism may provide more clarity regarding genetic factors shared by different autistic symptom domains than twin studies afford[245]. Last, sensory behaviours should be assessed in genetic studies of the autistic phenotype, as they are now included in the diagnostic criteria of autism and show clear experimental links to social and communicative traits[12].

In the meantime, we suggest it may be premature to give up on the hypothesis that symptoms of autism in different domains spring from common neurobiological and genetic origins.

Sensory-first accounts

Sensory-first accounts, which are motivated in part by studies of sensory deprivation during child institutionalization[182,183], hold that atypical sensory processing during early development causally stunts typical development of social cognition, in a feedforward manner. After all, dynamic sensory information is the medium of social communication: subtle fluctuations in the pitch of spoken language cue prosody, coordinated motions of the face communicate emotions and cues relevant to empathy[184], and the preparatory motions of a person's body relative to other objects in the world communicate intentions and requests[185]. Thus, a child who struggles to integrate dynamic sensory information may also struggle to build social information into meaningful representations or, alternatively, may find social information confusing and therefore self-select away from exposure or engagement with social information[186,187]. As discussed above, this hypothesis seems consistent with recent findings in animals[124].

Elegant research on the relationship between multisensory binding deficits and language processing in autism supports such a feedforward causal link. The ability to perceptually bind sensory signals across auditory and visual senses is fundamental to language perception, as it facilitates the integration of vocal and facial cues[188]. As discussed above, individuals with autism often show reduced multisensory binding[66], particularly for social stimuli (such as faces and voices)[72,83]. Furthermore, altered audiovisual binding thresholds in autism predict less-robust integration of visual and auditory signals of spoken language in tests of the McGurk effect[189] as well as a lower ability to accurately perceive speech in a noisy auditory environment[84]. These studies clearly illustrate how differences in basic sensory processing might affect the development of higher-order functions such as language perception.

Sensory-first accounts have strong merits but also shortcomings. First, among verbal individuals with autism, differences in language processing compared with that in neurotypical controls particularly peak in the domain of pragmatics[190], but why sensory differences would particularly affect this feature is not clear. Second, the neural basis of theory of mind is comparable in blind and sighted individuals, suggesting its development does not depend on typical sensory experience[191]. Thus, although sensory-first views may account for difficulties in certain aspects of language development, it is difficult to explain top-level autistic deficits in theory of mind from cascading difficulties in building stable sensory representations.

Top-down accounts

Top-down accounts posit that a centralized deficit in domain-general cognitive processes (such as attention, decision-making or causal inference) underpins deficits in both sensory and social-cognitive processing in autism. One instantiation of this theory is the 'weak central coherence' hypothesis, which posits that autistic neurobiology is characterized by a centralized perturbation of neural processes that aggregate information

(sensory or cognitive) into coherent percepts or cognitions[192]. In this account, sensory signalling is presumed to be unaffected in the autistic brain; rather, a higher-order mechanism that integrates these representations is altered. A neurobiological realization of such a theory would be, for example, deficits in association areas of the brain, where multimodal sensory representations are integrated with task demands.

However, top-down accounts such as the weak central coherence hypothesis are not immediately compatible with the empirical findings of alterations in low-level sensory cortex discussed above. It is particularly challenging to use top-down accounts to explain the neuroanatomical observations of altered minicolumn architecture in not only the association cortices but also the primary auditory cortex of post-mortem autistic brains[109]. It is therefore unlikely that centralized cognitive accounts will be able to provide a unifying factor for autistic symptoms in sensory and higher-order cognition.

Canonical micro-circuitry view

We turn now to a third hypothesis, which we call the canonical micro-circuitry view. This view is largely inspired by genetic studies in autism that implicate changes in synaptic connectivity, signalling and plasticity in the condition[163]. Such low-level changes would not necessarily be confined to particular cortical regions (such as the 'social brain') but would be predicted to affect basic components of neural circuits throughout the brain[163]. Given that many cortical regions share neural motifs[14,193] that participate in common canonical computations, genetic disruption of neural motifs might affect many regions of the brain and produce structurally similar behavioural traits in various perceptual and cognitive domains[194].

In addition to divisive normalization (mentioned above), another candidate neural motif-mediated computation that has recently been implicated in autism is Bayesian perceptual inference. Bayesian inference has been shown to be implemented in every neural domain, including sensory perception[195], motor planning[196], language[197], social cognition[198] and proprioception[199]. Individuals with autism have been posited to have perceptual representations in which bottom-up sensory input is weighted more than top-down predictions[181]. Other theories challenge this hypothesis, holding that autistic perception could instead be characterized by imprecise sensory representations[200], aberrant weighting of sensory prediction errors[201] or aberrant updating of priors[202]. Compellingly, one recent study shows a reduced reliance on implicitly learned priors when discriminating sensory representations in a volatile environment, an effect that is reflected in reduced measures of surprise, as derived from pupil dilation, in individuals with autism[203]. Further empirical studies of autistic behaviour are needed to disentangle these hypotheses and to specify the levels of cortical processing at which Bayesian inference might be altered in autism. However, the rubric of Bayesian inference presents the opportunity to test whether systematic failures of a common computational principle might account for different domains of autistic symptomatology. For example, can weaker priors aptly describe autistic performance on sensory, pragmatic-language and social-cognitive tasks?

How might we go about identifying altered neural motifs in autism? We suggest that this is a two-part endeavour that involves both human and animal model research. In human research, we might start by identifying behavioural paradigms in which similar differences in autism can be observed across different domains of processing (for example, in perception, language and cognition) and that might therefore engage a common neural motif. One example of such a task might be ambiguity resolution. In visual perception, individuals with autism are slower than controls to resolve low-level perceptual ambiguity of two conflicting inputs presented to the two eyes (binocular rivalry)[127,132,133]. Similarly, in pragmatic language, when presented with sentences containing words that could have two meanings (for example, homographs such as 'bow' or 'bass'), children with autism struggle to resolve this ambiguity, failing to use the sentence context to inform their pronunciation and often defaulting to the more common pronunciation[204,205]. Ambiguity resolution in both domains of representation — in visual perception and in language — may plausibly rely on neural motifs consisting of reciprocal inhibitory competitive interactions between neural populations that vie for perceptual representation[206,207].

Such a motif may even be a neural substrate of theory-of-mind challenges in autism[1]: during theory-of-mind judgements, the child must co-activate and flexibly alternate between two, sometimes conflicting, representations of the world — their own understanding and another person's — to navigate social interactions. Interestingly, the ability to resolve ambiguity in perception (during perceptual bistability), in language (homograph understanding) and in social cognition (theory of mind) tends to develop at approximately the fourth year of life[208,209]. Furthermore, individual differences in the onset of these abilities correlate across domains[209,210], suggesting that ambiguity resolution across these processing domains may be linked. Notably, in children with autism, individual differences in perceptual bistability predict theory-of-mind performance and ADOS scores[127,132,209].

Once a potential neural motif has been identified in humans, animal model research may help to identify specific disruptions in neural circuitry that underpin this motif (FIG. 3). When animal model research implicates a specific neurotransmitter pathway, human neuroimaging studies using MRS or positron emission tomography can probe the integrity of this pathway in humans and test whether it underpins behavioural differences. Finally, a crucial step will be to test whether genetic animal models of autism recapitulate the observed human-behavioural differences. Given the relative ease of translating sensory behavioural findings between humans and animal models, further research into symptoms of autism in the sensory domain may lead to promising translational opportunities.

Neural motifs
Stereotyped, local neural circuits that are found in multiple regions of the brain and participate in common canonical computations (such as habituation, response normalization or biased competition).

Bayesian perceptual inference
A model of perception in which prior knowledge about a stimulus is combined with noisy, stimulus-evoked sensory signals to infer the percept and generate prediction errors.

Ambiguity resolution
The ability to impose meaning on ambiguous sensory information. Two or more interpretations may be equally viable (as in bistable visual phenomena, such as in binocular rivalry) or can be disambiguated using contextual information.

Looking forward

This Review posits that sensory symptoms are core, primary characteristics of the neurobiology of autism. Specifically, sensory processing differences in autism are visible early in development[211–213], as early as infancy[16], and are predictive of diagnostic status later in childhood[19,38,39]. They predict higher-order deficits in social and cognitive function in adults[178,214] and explain independent variance in social and communication symptoms in diagnostic assessments[215]. Moreover, autism-associated sensory symptoms reflect alterations in sensory-dedicated neural circuitry[59,100], including neuromolecular and anatomical changes in primary sensory regions of the brain[64,109,127], rather than secondary consequences of alterations in higher-order cognitive processes. These differences manifest in both humans and genetic animal models of autism, in which GABAergic signalling is often commonly affected[64,76,123,124,127], holding promise for translational biomarkers of the condition.

This conclusion marks a revolutionary shift in our conception of autism from its early diagnostic characterizations[13] and calls into question modern 'social brain' theories[15], in which sensory deficits are hypothesized to be epiphenomenal to core deficits in social processing. Moving forward, neurobiological theories of autism must account for atypical processing in both social and sensory domains.

One of the biggest challenges to formulating neurobiological theories of autism has been the persistent difficulty of documenting robust, replicable differences between individuals with autism and controls, even with simple tests of sensory processing. Given the genetic heterogeneity of the autistic population, one promising contribution of sensory paradigms may be the ability to stratify the autistic population into more homogeneous subgroups of individuals who share common underlying neurobiological alterations, such as on the basis of sensory differences that are associated with certain genetic polymorphisms[216,217]. Indeed, sensory subtypes are often reported in children with autism in clinical surveys[218]. Identifying and characterizing such subgroups in the laboratory setting will require the analysis of larger samples than are typically used. In the meantime, replications in independent samples of participants and a number of statistical practices must be used to ensure meaningful between-group comparisons, including using nonparametric statistics when data violate assumptions of normality, bootstrapping statistical comparisons to minimize the effects of outliers, matching groups on relevant psychophysical factors, and eye tracking when retinal position is a relevant variable for task performance.

Autism affects every domain of human experience: from sensation and perception to motor behaviour, emotion, communication and cognition. A central challenge of autism research is to understand how these disparate domains might be related. We suggest that research on sensory symptoms may be able to help untangle this complexity, shedding light on circuit-level alterations in the brain that might affect various domains of cortical processing in autism and offering avenues for translational research.

1. Baron-Cohen, S., Leslie, A. M. & Frith, U. Does the autistic child have a 'theory of mind'? *Cognition* **21**, 37–46 (1985).
2. Baron-Cohen, S. & Wheelwright, S. The empathy quotient: an investigation of adults with Asperger syndrome or high functioning autism, and normal sex differences. *J. Autism Dev. Disord.* **34**, 163–175 (2004).
3. Tomchek, S. D. & Dunn, W. Sensory processing in children with and without autism: a comparative study using the Short Sensory Profile. *Am. J. Occup. Ther.* **61**, 190–200 (2007).
4. Tavassoli, T., Miller, L. J., Schoen, S. A., Nielsen, D. M. & Baron-Cohen, S. Sensory over-responsivity in adults with autism spectrum conditions. *Autism* **18**, 428–432 (2014).
5. Tavassoli, T. & Baron-Cohen, S. Taste identification in adults with autism spectrum conditions. *J. Autism Dev. Disord.* **42**, 1419–1424 (2012).
6. Marco, E. J. *et al.* Children with autism show reduced somatosensory response: an MEG study. *Autism Res.* **5**, 340–351 (2012).
7. Puts, N. A. J., Wodka, E. L., Tommerdahl, M., Mostofsky, S. H. & Edden, R. A. E. Impaired tactile processing in children with autism spectrum disorder. *J. Neurophysiol.* **111**, 1803–1811 (2014).
8. Bonnel, A. *et al.* Enhanced pitch sensitivity in individuals with autism: a signal detection analysis. *J. Cogn. Neurosci.* **15**, 226–235 (2003).
9. Galle, S., Courchesne, V., Mottron, L. & Frasnelli, J. Olfaction in the autism spectrum. *Perception* **42**, 341–355 (2013).
10. Rozenkrantz, L. *et al.* A mechanistic link between olfaction and autism spectrum disorder. *Curr. Biol.* **25**, 1904–1910 (2015).
11. Simmons, D. R. *et al.* Vision in autism spectrum disorders. *Vision Res.* **49**, 2705–2739 (2009).
12. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders (DSM-5)* 5th edn (American Psychiatric Association, 2013).
13. Kanner, L. Autistic disturbances of affective contact. *Nerv. Child* **2**, 217–250 (1943).
14. Heeger, D. J., Behrmann, M. & Dinstein, I. Vision as a beachhead. *Biol. Psychiatry* **81**, 832–837 (2016).
15. Pelphrey, K. A., Shultz, S., Hudac, C. M. & Vander Wyk, B. C. Research review: constraining heterogeneity: the social brain and its development in autism spectrum disorder. *J. Child Psychol. Psychiatry* **52**, 631–644 (2011).
16. Baranek, G. T. *et al.* Hyporesponsiveness to social and nonsocial sensory stimuli in children with autism, children with developmental delays, and typically developing children. *Dev. Psychopathol.* **25**, 307–320 (2013).
17. Estes, A. *et al.* Behavioral, cognitive, and adaptive development in infants with autism spectrum disorder in the first 2 years of life. *J. Neurodev. Disord.* **7**, 24 (2015).
This longitudinal study of infants at risk of autism diagnoses shows that high-risk infants have higher levels of sensorimotor symptoms at 6 months of age and that these symptoms predict subsequent diagnostic status..
18. Brooks, R. & Meltzoff, A. N. The importance of eyes: how infants interpret adult looking behavior. *Dev. Psychol.* **38**, 958–966 (2002).
19. Turner-Brown, L. M., Baranek, G. T., Reznick, J. S., Watson, L. R. & Crais, E. R. The First Year Inventory: a longitudinal follow-up of 12-month-old to 3-year-old children. *Autism* **17**, 527–540 (2013).
20. Boyd, B. A. *et al.* Sensory features and repetitive behaviors in children with autism and developmental delays. *Autism Res.* **3**, 78–87 (2010).
21. Donaldson, C. K., Stauder, J. E. A. & Donkers, F. C. L. Increased sensory processing atypicalities in parents of multiplex ASD families versus typically developing and simplex ASD families. *J. Autism Dev. Disord.* **47**, 535–548 (2017).
22. Glod, M., Riby, D. M., Honey, E. & Rodgers, J. Sensory atypicalities in dyads of children with autism spectrum disorder (ASD) and their parents. *Autism Res.* **10**, 531–538 (2017).
23. Mikkelsen, M., Wodka, E. L., Mostofsky, S. H. & Puts, N. A. J. Autism spectrum disorder in the scope of tactile processing. *Dev. Cogn. Neurosci.* http://dx.doi.org/10.1016/j.dcn.2016.12.005 (2017).
24. Haesen, B., Boets, B. & Wagemans, J. A review of behavioural and electrophysiological studies on auditory processing and speech perception in autism spectrum disorders. *Res. Autism Spectr. Disord.* **5**, 701–714 (2011).
25. Baum, S. H., Stevenson, R. A. & Wallace, M. T. Behavioral, perceptual, and neural alterations in sensory and multisensory function in autism spectrum disorder. *Prog. Neurobiol.* **134**, 140–160 (2015).
26. Stevenson, R. A. *et al.* Keeping time in the brain: autism spectrum disorder and audiovisual temporal processing. *Autism Res.* **9**, 720–738 (2016).
27. Wallace, M. T. & Stevenson, R. A. The construct of the multisensory temporal binding window and its dysregulation in developmental disabilities. *Neuropsychologia* **64**, 105–123 (2014).
28. Shah, A. & Frith, U. An islet of ability in autistic children: a research note. *J. Child Psychol. Psychiatry* **24**, 613–620 (1983).
29. Happe, F., Briskman, J. & Frith, U. Exploring the cognitive phenotype of autism: weak 'central coherence' in parents and siblings of children with autism. Experimental tests. I. *J. Child Psychol. Psychiatry* **42**, 309–316 (2001).
30. Baron-Cohen, S., Ashwin, E., Ashwin, C., Tavassoli, T. & Chakrabarti, B. Talent in autism: hyper-systemizing, hyper-attention to detail and sensory hypersensitivity. *Phil. Trans. R. Soc. Lond. B Biol. Sci.* **364**, 1377–1383 (2009).
31. Plaisted, K., O'Riordan, M. & Baron-Cohen, S. Enhanced visual search for a conjunctive target in autism: a research note. *J. Child Psychol. Psychiatry* **39**, 777–783 (1998).
This foundational study shows faster target detection during conjunctive visual search in autism — a finding now widely replicated.

32. Plaisted, K., O'Riordan, M. & Baron-Cohen, S. Enhanced discrimination of novel, highly similar stimuli by adults with autism during a perceptual learning task. *J. Child Psychol. Psychiatry* **39**, 765–775 (1998).
33. O'Riordan, M. A., Plaisted, K. C., Driver, J. & Baron-Cohen, S. Superior visual search in autism. *J. Exp. Psychol. Hum. Percept. Perform.* **27**, 719–730 (2001).
34. Keehn, B., Brenner, L., Palmer, E., Lincoln, A. J. & Müller, R.-A. Functional brain organization for visual search in ASD. *J. Int. Neuropsychol. Soc.* **14**, 990–1003 (2008).
35. Baldassi, S. *et al.* Search superiority in autism within, but not outside the crowding regime. *Vision Res.* **49**, 2151–2156 (2009).
36. Joseph, R. M., Keehn, B., Connolly, C., Wolfe, J. M. & Horowitz, T. S. Why is visual search superior in autism spectrum disorder? *Dev. Sci.* **12**, 1083–1096 (2009).
37. Kéïta, L., Mottron, L. & Bertone, A. Far visual acuity is unremarkable in autism: do we need to focus on crowding? *Autism Res.* **3**, 333–341 (2010).
38. Gliga, T., Bedford, R., Charman, T. & Johnson, M. H. Enhanced visual search in infancy predicts emerging autism symptoms. *Curr. Biol.* **25**, 1727–1730 (2015).
39. Kaldy, Z., Kraper, C., Carter, A. S. & Blaser, E. Toddlers with autism spectrum disorder are more successful at visual search than typically developing toddlers. *Dev. Sci.* **14**, 980–988 (2011).
40. Wang, S. *et al.* Atypical visual saliency in autism spectrum disorder quantified through model-based eye tracking. *Neuron* **88**, 604–616 (2015).
This data-driven analysis of gaze patterns during natural scene-viewing in individuals with autism shows that gaze patterns in autism are biased towards scene regions that are salient in terms of low-level pixel features (such as contrast, colour and orientation).
41. Mottron, L., Dawson, M., Soulières, I., Hubert, B. & Burack, J. Enhanced perceptual functioning in autism: an update, and eight principles of autistic perception. *J. Autism Dev. Disord.* **36**, 27–43 (2006).
42. Tavassoli, T., Latham, K., Bach, M., Dakin, S. C. & Baron-Cohen, S. Psychophysical measures of visual acuity in autism spectrum conditions. *Vision Res.* **51**, 1778–1780 (2011).
43. de Jonge, M. V. *et al.* Visual information processing in high-functioning individuals with autism spectrum disorders and their parents. *Neuropsychology* **21**, 65–73 (2007).
44. Koh, H. C., Milne, E. & Dobkins, K. Spatial contrast sensitivity in adolescents with autism spectrum disorders. *J. Autism Dev. Disord.* **40**, 978–987 (2010).
45. Freyberg, J., Robertson, C. E. & Baron-Cohen, S. Typical magnitude and spatial extent of crowding in autism. *J. Vis.* **16**, 17 (2016).
46. Grubb, M. A. *et al.* Endogenous spatial attention: evidence for intact functioning in adults with autism. *Autism Res.* **6**, 108–118 (2013).
47. Bertone, A., Mottron, L., Jelenic, P. & Faubert, J. Enhanced and diminished visuo-spatial information processing in autism depends on stimulus complexity. *Brain* **128**, 2430–2441 (2005).
48. Pellicano, E., Gibson, L., Maybery, M., Durkin, K. & Badcock, D. R. Abnormal global processing along the dorsal visual pathway in autism: a possible mechanism for weak visuospatial coherence? *Neuropsychologia* **43**, 1044–1053 (2005).
49. Kéïta, L., Guy, J., Berthiaume, C., Mottron, L. & Bertone, A. An early origin for detailed perception in autism spectrum disorder: biased sensitivity for high-spatial frequency information. *Sci. Rep.* **4**, 5475 (2014).
50. Caplette, L., Wicker, B. & Gosselin, F. Atypical time course of object recognition in autism spectrum disorder. *Sci. Rep.* **6**, 35494 (2016).
51. Van der Hallen, R. Evers, K., Brewaeys, K., Van den Noortgate, W. & Wagemans, J. Global processing takes time: a meta-analysis on local–global visual processing in ASD. *Psychol. Bull.* **141**, 549–573 (2015).
52. Blake, R., Turner, L. M., Smoski, M. J., Pozdol, S. L. & Stone, W. L. Visual recognition of biological motion is impaired in children with autism. *Psychol. Sci.* **14**, 151–157 (2003).
53. Spencer, J. *et al.* Motion processing in autism: evidence for a dorsal stream deficiency. *Neuroreport* **11**, 2765–2767 (2000).
54. Koh, H. C., Milne, E. & Dobkins, K. Contrast sensitivity for motion detection and direction discrimination in adolescents with autism spectrum disorders and their siblings. *Neuropsychologia* **48**, 4046–4056 (2010).
55. Koldewyn, K., Whitney, D. & Rivera, S. M. The psychophysics of visual motion and global form processing in autism. *Brain* **133**, 599–610 (2010).
56. Manning, C. *et al.* Enhanced integration of motion information in children with autism. *J. Neurosci.* **35**, 6979–6986 (2015).
57. Chen, Y. *et al.* Enhanced local processing of dynamic visual information in autism: evidence from speed discrimination. *Neuropsychologia* **50**, 733–739 (2012).
58. Robertson, C. E., Martin, A., Baker, C. I. & Baron-Cohen, S. Atypical integration of motion signals in autism spectrum conditions. *PLoS ONE* **7**, e48173 (2012).
59. Robertson, C. E. *et al.* Global motion perception deficits in autism are reflected as early as primary visual cortex. *Brain* **137**, 2588–2599 (2014).
60. Güçlü, B., Tanidir, C., Mukaddes, N. M. & Ünal, F. Tactile sensitivity of normal and autistic children. *Somatosens. Mot. Res.* **24**, 21–33 (2007).
61. O'Riordan, M. & Passetti, F. Discrimination in autism within different sensory modalities. *J. Autism Dev. Disord.* **36**, 665–675 (2006).
62. Blakemore, S. *et al.* Tactile sensitivity in Asperger syndrome. *Brain Cogn* **61**, 5–13 (2006).
63. Tavassoli, T. *et al.* Altered tactile processing in children with autism spectrum disorder. *Autism Res.* **9**, 616–620 (2016).
64. Puts, N. A. J. *et al.* Reduced GABA and altered somatosensory function in children with autism spectrum disorder. *Autism Res.* **10**, 608–619 (2017).
65. Khan, S. *et al.* Somatosensory cortex functional connectivity abnormalities in autism show opposite trends, depending on direction and spatial scale. *Brain* **138**, 1394–1409 (2015).
66. Kwakye, L. D., Foss-Feig, J. H., Cascio, C. J., Stone, W. L. & Wallace, M. T. Altered auditory and multisensory temporal processing in autism spectrum disorders. *Front. Integr. Neurosci.* **4**, 129 (2011).
67. Edgar, J. C. *et al.* Neuromagnetic oscillations predict evoked-response latency delays and core language deficits in autism spectrum disorders. *J. Autism Dev. Disord.* **45**, 395–405 (2013).
68. Roberts, T. P. L. *et al.* MEG detection of delayed auditory evoked responses in autism spectrum disorders: towards an imaging biomarker for autism. *Autism Res.* **3**, 8–18 (2010).
69. Brandwein, A. B. *et al.* Neurophysiological indices of atypical auditory processing and multisensory integration are associated with symptom severity in autism. *J. Autism Dev. Disord.* **45**, 230–244 (2014).
70. Roberts, T. P. L. *et al.* Auditory magnetic mismatch field latency: a biomarker for language impairment in autism. *Biol. Psychiatry* **70**, 263–269 (2011).
71. Oram Cardy, J. E., Flagg, E. J., Roberts, W. & Roberts, T. P. L. Auditory evoked fields predict language ability and impairment in children. *Int. J. Psychophysiol.* **68**, 170–175 (2008).
72. Stevenson, R. A., Segers, M., Ferber, S., Barense, M. D. & Wallace, M. T. The impact of multisensory integration deficits on speech perception in children with autism spectrum disorders. *Front. Psychol.* **5**, 379 (2014).
This is a recent review of evidence for robust multi-sensory-integration deficits in autism and their implications for difficulties in language development.
73. Bebko, J. M., Weiss, J. A., Demark, J. L. & Gomez, P. Discrimination of temporal synchrony in intermodal events by children with autism and children with developmental disabilities without autism. *J. Child Psychol. Psychiatry* **47**, 88–98 (2006).
74. Stevenson, R. A. *et al.* Multisensory temporal integration in autism spectrum disorders. *J. Neurosci.* **34**, 691–697 (2014).
75. Stevenson, R. A. *et al.* Evidence for diminished multisensory integration in autism spectrum disorders. *J. Autism Dev. Disord.* **44**, 3161–3167 (2014).
76. Gogolla, N., Takesian, A. E., Feng, G., Fagiolini, M. & Hensch, T. K. Sensory integration in mouse insular cortex reflects GABA circuit maturation. *Neuron* **83**, 894–905 (2014).
77. Jao Keehn, R. J. *et al.* Impaired downregulation of visual cortex during auditory processing is associated with autism symptomatology in children and adolescents with autism spectrum disorder. *Autism Res.* **10**, 130–143 (2017).
78. Collignon, O. *et al.* Reduced multisensory facilitation in persons with autism. *Cortex* **49**, 1704–1710 (2013).
79. Siemann, J. K. *et al.* An autism-associated serotonin transporter variant disrupts multisensory processing. *Transl Psychiatry* **7**, e1067 (2017).
80. Noel, J. P., De Niear, M. A., Stevenson, R., Alais, D. & Wallace, M. T. Atypical rapid audio-visual temporal recalibration in autism spectrum disorders. *Autism Res.* **10**, 121–129 (2017).
81. Brandwein, A. B. *et al.* The development of multisensory integration in high-functioning autism: high-density electrical mapping and psychophysical measures reveal impairments in the processing of audiovisual inputs. *Cereb. Cortex* **23**, 1329–1341 (2013).
82. Stevenson, R. A. *et al.* Multisensory speech perception in autism spectrum disorder: From phoneme to whole-word perception. *Autism Res.* **10**, 1280–1290 (2017).
83. Foxe, J. J. *et al.* Severe multisensory speech integration deficits in high-functioning school-aged children with autism spectrum disorder (ASD) and their resolution during early adolescence. *Cereb. Cortex* **25**, 298–312 (2015).
84. Stevenson, R. A. *et al.* The cascading influence of multisensory processing on speech perception in autism. *Autism* http://dx.doi.org/10.1177/1362361317704413 (2017).
85. Brock, J., Brown, C. C., Boucher, J. & Rippon, G. The temporal binding deficit hypothesis of autism. *Dev. Psychopathol.* **14**, 209–224 (2002).
86. Nakayama, K. & Silverman, G. H. Serial and parallel processing of visual feature conjunctions. *Nature* **320**, 264–265 (1986).
87. Churchland, A. K., Kiani, R. & Shadlen, M. N. Decision-making with multiple alternatives. *Nat. Neurosci.* **11**, 693–702 (2008).
88. Magnotti, J. F., Ma, W. J. & Beauchamp, M. S. Causal inference of asynchronous audiovisual speech. *Front. Psychol.* **4**, 798 (2013).
89. Shadlen, M. N. & Newsome, W. T. Motion perception: seeing and deciding. *Proc. Natl Acad. Sci. USA* **93**, 628–633 (1996).
90. Mikami, A., Newsome, W. T. & Wurtz, R. H. Motion selectivity in macaque visual cortex. I. Mechanisms of direction and speed selectivity in extrastriate area MT. *J. Neurophysiol.* **55**, 1308–1327 (1986).
91. Snowden, R. J., Treue, S., Erickson, R. G. & Andersen, R. The response of area MT and V1 neurons to transparent motion. *J. Neurosci.* **11**, 2768–2785 (1991).
92. Zaidel, A., Goin-Kochel, R. P. & Angelaki, D. E. Self-motion perception in autism is compromised by visual noise but integrated optimally across multiple senses. *Proc. Natl Acad. Sci. USA* **112**, 6461–6466 (2015).
93. Manning, C., Charman, T. & Pellicano, E. Processing slow and fast motion in children with autism spectrum conditions. *Autism Res.* **6**, 531–541 (2013).
94. Takarae, Y., Luna, B., Minshew, N. J. & Sweeney, J. A. Visual motion processing and visual sensorimotor control in autism. **20**, 113–122 (2014).
95. Peiker, I. *et al.* Stronger neural modulation by visual motion intensity in autism spectrum disorders. *PLoS ONE* **10**, 1–17 (2015).
96. Herrington, J. D. *et al.* The role of MT + /V5 during biological motion perception in Asperger Syndrome: an fMRI study. *Res. Autism Spectr. Disord.* **1**, 14–27 (2007).
97. Greimel, E. *et al.* The temporal dynamics of coherent motion processing in autism spectrum disorder: evidence for a deficit in the dorsal pathway. *Behav. Brain Res.* **251**, 168–175 (2013).
98. Koldewyn, K., Whitney, D. & Rivera, S. M. Neural correlates of coherent and biological motion perception in autism. *Dev. Sci.* **14**, 1075–1088 (2011).
99. Milne, E. Increased intra-participant variability in children with autistic spectrum disorders: evidence from single-trial analysis of evoked EEG. *Front. Psychol.* **2**, 51 (2011).
100. Dinstein, I. *et al.* Unreliable evoked responses in autism. *Neuron* **75**, 981–991 (2012).
This key study shows that, although the magnitude of evoked responses to sensory stimuli is typical in autism, the signal-to-noise ratio of sensory responses is poor, owing to higher intra-subject variance in the response amplitude in autism.
101. Haigh, S. M., Minshew, N., Heeger, D. J., Dinstein, I. & Behrmann, M. Over-responsiveness and greater variability in roughness perception in autism. **9**, 393–402 (2016).
102. Butler, J. S., Molholm, S., Andrade, G. N. & Foxe, J. J. An examination of the neural unreliability thesis of autism. *Cereb. Cortex* **27**, 1–16 (2017).

103. Haigh, S. M. *et al.* Differential sensory fMRI signatures in autism and schizophrenia: analysis of amplitude and trial-to-trial variability. *Schizophr. Res.* **175**, 12–19 (2016).
104. Shen, W., McKeown, C. R., Demas, J. A. & Cline, H. T. Inhibition to excitation ratio regulates visual system responses and behavior *in vivo*. *J. Neurophysiol.* **106**, 2285–2302 (2011).
105. Schwarzkopf, D. S. *et al.* Larger extrastriate population receptive fields in autism spectrum disorders. *J. Neurosci.* **34**, 2713–2724 (2014).
106. Baron-Cohen, S. *et al.* Is synaesthesia more common in autism? *Mol. Autism* **4**, 40 (2013).
107. Kastner, S., De Weerd, P., Desimone, R. & Ungerleider, L. Mechanisms of directed attention in the human extrastriate cortex as revealed by functional MRI. *Science* **282**, 108–111 (1998).
108. Silver, M. A., Ress, D. & Heeger, D. J. Neural correlates of sustained spatial attention in human early visual cortex. *J. Neurophysiol.* **97**, 229–237 (2007).
109. Mckavanagh, R., Buckley, E. & Chance, S. A. Wider minicolumns in autism: a neural basis for altered processing? *Brain* **138**, 2034–2045 (2015).
This recent, large post-mortem study observed wider minicolumns in the brains of individuals; this alteration to a basic building block of neural architecture affects both primary sensory cortex (A1) and higher-order association areas.
110. Casanova, M. F. *et al.* Minicolumnar abnormalities in autism. *Acta Neuropathol.* **112**, 287–303 (2006).
111. Ronconi, L., Gori, S., Ruffino, M., Molteni, M. & Facoetti, A. Zoom-out attentional impairment in children with autism spectrum disorder. *Cortex* **49**, 1025–1033 (2013).
112. Robertson, C. E., Kravitz, D. J., Freyberg, J., Baron-Cohen, S. & Baker, C. I. Tunnel vision: sharper gradient of spatial attention in autism. *J. Neurosci.* **33**, 6776–6781 (2013).
113. Koldewyn, K., Weigelt, S., Kanwisher, N. & Jiang, Y. Multiple object tracking in autism spectrum disorders. *J. Autism Dev. Disord.* **43**, 1394–1405 (2013).
114. Grubb, M. A. *et al.* Exogenous spatial attention: evidence for intact functioning in adults with autism spectrum disorder. *J. Vis.* **13**, 9 (2013).
115. Canitano, R. Epilepsy in autism spectrum disorders. *Eur. Child Adolesc. Psychiatry* **16**, 61–66 (2007).
116. Sanders, S. J. *et al.* Multiple recurrent *de novo* CNVs, including duplications of the 7q11.23 Williams syndrome region, are strongly associated with autism. *Neuron* **70**, 863–885 (2011).
117. Griswold, A. J. *et al.* Evaluation of copy number variations reveals novel candidate genes in autism spectrum disorder-associated pathways. *Hum. Mol. Genet.* **21**, 3513–3523 (2012).
118. Shao, Y. *et al.* Fine mapping of autistic disorder to chromosome 15q11-q13 by use of phenotypic subtypes. *Am. J. Hum. Genet.* **72**, 539–548 (2003).
119. Ma, D. Q. *et al.* Identification of significant association and gene-gene interaction of GABA receptor subunit genes in autism. *Am. J. Hum. Genet.* **77**, 377–388 (2005).
120. Chen, C. H. *et al.* Genetic analysis of *GABRB3* as a candidate gene of autism spectrum disorders. *Mol. Autism* **5**, 36 (2014).
121. Piton, A. *et al.* Analysis of the effects of rare variants on splicing identifies alterations in $GABA_A$ receptor genes in autism spectrum disorder individuals. *Eur. J. Hum. Genet.* **21**, 749–756 (2013).
122. Fatemi, S. H., Reutiman, T. J., Folsom, T. D. & Thuras, P. D. $GABA_A$ receptor downregulation in brains of subjects with autism. *J. Autism Dev. Disord.* **39**, 223–230 (2009).
123. Gogolla, N. *et al.* Common circuit defect of excitatory–inhibitory balance in mouse models of autism. *J. Neurodev. Disord.* **1**, 172–181 (2009).
This study provides insights into common circuit-level differences observed in multiple mouse models of autism with distinct genetic origins, by reporting a reduction in parvalbumin-expressing inhibitory neurons across parietal and occipital cortex.
124. Orefice, L. L. *et al.* Peripheral mechanosensory neuron dysfunction underlies tactile and behavioral deficits in mouse models of ASDs. *Cell* **166**, 299–313 (2016).
This new study demonstrates that several mouse models of autism exhibit tactile hypersensitivities, which arise from disruptions to $GABA_A$R-mediated inhibition.
125. Turkheimer, F. E., Leech, R., Expert, P., Lord, L.-D. & Vernon, A. C. The brain's code and its canonical computational motifs. From sensory cortex to the default mode network, a multi-scale model of brain function in health and disease. *Neurosci. Biobehav. Rev.* **55**, 211–222 (2015).
126. Hensch, T. K. Critical period plasticity in local cortical circuits. *Nat. Rev. Neurosci.* **6**, 877–888 (2005).
127. Robertson, C. E., Ratai, E. M. & Kanwisher, N. Reduced GABAergic action in the autistic brain. *Curr. Biol.* **26**, 80–85 (2016).
This recent study links a replicated autistic visual deficit in binocular rivalry to disrupted GABAergic, but preserved glutamatergic, action in the autistic visual cortex.
128. Laing, C. R. & Chow, C. C. A spiking neuron model for binocular rivalry. *J. Comput. Neurosci.* **12**, 39–53 (2002).
129. Seely, J. & Chow, C. C. Role of mutual inhibition in binocular rivalry. **106**, 2136–2150 (2012).
130. Said, C. P. & Heeger, D. J. A model of binocular rivalry and cross-orientation suppression. *PLoS Comput. Biol.* **9**, e1002991 (2013).
131. Van Loon, A. M. *et al.* GABA shapes the dynamics of bistable perception. *Curr. Biol.* **23**, 823–827 (2013).
132. Robertson, C. E., Kravitz, D. J., Freyberg, J., Baron-Cohen, S. & Baker, C. I. Slower rate of binocular rivalry in autism. *J. Neurosci.* **33**, 16983–16991 (2013).
133. Freyberg, J., Robertson, C. E. & Baron-Cohen, S. Reduced perceptual exclusivity during object and grating rivalry in autism. *J. Vis.* **15**, 11 (2015).
134. Foss-Feig, J. H., Tadin, D., Schauder, K. B. & Cascio, C. J. A substantial and unexpected enhancement of motion perception in autism. *J. Neurosci.* **33**, 8243–8249 (2013).
135. Sysoeva, O. V., Galuta, I. A., Davletshina, M. S., Orekhova, E. V. & Stroganova, T. A. Abnormal size-dependent modulation of motion perception in children with autism spectrum disorder (ASD). *Front. Neurosci.* **11**, 164 (2017).
136. Haigh, S. M., Heeger, D. J., Dinstein, I., Minshew, N. & Behrmann, M. Cortical variability in the sensory-evoked response in autism. *J. Autism Dev. Disord.* **45**, 1176–1190 (2014).
137. Schauder, K. B., Park, W. J., Tadin, D. & Bennetto, L. Larger receptive field size as a mechanism underlying atypical motion perception in autism spectrum disorder. *Clin. Psychol. Sci.* http://dx.doi.org/10.1177/2167702617707733 (2017).
138. Thiele, A., Herrero, J. L., Distler, C. & Hoffmann, K. P. Contribution of cholinergic and GABAergic mechanisms to direction tuning, discriminability, response reliability, and neuronal rate correlations in macaque middle temporal area. *J. Neurosci.* **32**, 16602–16615 (2012).
139. Lund, J. S., Wu, Q., Hadingham, P. T. & Levitt, J. B. Cells and circuits contributing to functional properties in area V1 of macaque monkey cerebral cortex: bases for neuroanatomically realistic models. *J. Anat.* **187**, 563–581 (1995).
140. Yip, J., Soghomonian, J. J. & Blatt, G. J. Decreased GAD67 mRNA levels in cerebellar Purkinje cells in autism: pathophysiological implications. *Acta Neuropathol.* **113**, 559–568 (2007).
141. Blatt, G. J. *et al.* Density and distribution of hippocampal neurotransmitter receptors in autism: an autoradiographic study. *J. Autism Dev. Disord.* **31**, 537–543 (2001).
142. Fatemi, S. H., Folsom, T. D., Reutiman, T. J. & Thuras, P. D. Expression of $GABA_B$ receptors is altered in brains of subjects with autism. *Cerebellum* **8**, 64–69 (2009).
143. Collins, A. L. *et al.* Investigation of autism and GABA receptor subunit genes in multiple ethnic groups. *Neurogenetics* **7**, 167–174 (2006).
144. Menold, M. M. *et al.* Association analysis of chromosome 15 $GABA_A$ receptor subunit genes in autistic disorder. *J. Neurogenet.* **15**, 245–259 (2001).
145. Ben-Ari, Y. Is birth a critical period in the pathogenesis of autism spectrum disorders? *Nat. Rev. Neurosci.* **16**, 498–505 (2015).
146. Dorrn, A. L., Yuan, K., Barker, A. J., Schreiner, C. E. & Froemke, R. C. Developmental sensory experience balances cortical excitation and inhibition. *Nature* **465**, 932–936 (2010).
147. Shibata, K. *et al.* Overlearning hyperstabilizes a skill by rapidly making neurochemical processing inhibitory-dominant. *Nat. Neurosci.* **20**, 470–475 (2017).
148. Zheng, Z. *et al.* Blood glutamate levels in autism spectrum disorder: a systematic review and meta-analysis. *PLoS ONE* **11**, e0158688 (2016).
149. Fatemi, S. H., Folsom, T. D., Kneeland, R. E. & Liesch, S. B. Metabotropic glutamate receptor 5 upregulation in children with autism is associated with underexpression of both fragile X mental retardation protein and $GABA_A$ receptor beta 3 in adults with autism. *Anat. Rec. (Hoboken)* **294**, 1635–1645 (2011).
150. Zhang, L. *et al.* The expression of $GABA_A$ receptor $\alpha 2$ subunit is upregulated by testosterone in rat cerebral cortex. *Neurosci. Lett.* **265**, 25–28 (1999).
151. Harden, S. W. & Frazier, C. J. Oxytocin depolarizes fast-spiking hilar interneurons and induces GABA release onto mossy cells of the rat dentate gyrus. *Hippocampus* **26**, 1124–1139 (2016).
152. Owen, S. F. *et al.* Oxytocin enhances hippocampal spike transmission by modulating fast-spiking interneurons. *Nature* **500**, 458–462 (2013).
153. Baron-Cohen, S. *et al.* Why are autism spectrum conditions more prevalent in males? *PLoS Biol.* **9**, e1001081 (2011).
154. Baron-Cohen, S. *et al.* Elevated fetal steroidogenic activity in autism. *Mol. Psychiatry* **20**, 369–376 (2015).
155. Gordon, I. *et al.* Oxytocin enhances brain function in children with autism. *Proc. Natl Acad. Sci. USA* **110**, 20953–20958 (2013).
156. Rubenstein, J. L. R. & Merzenich, M. M. Model of autism: increased ratio of excitation/inhibition in key neural systems. *Brain* **2**, 255–267 (2003).
157. Vattikuti, S. & Chow, C. A computational model for cerebral cortical dysfunction in autism spectrum disorders. *Biol. Psychiatry* **67**, 672–678 (2010).
158. Rosenberg, A., Patterson, J. S. & Angelaki, D. E. A computational perspective on autism. *Proc. Natl Acad. Sci. USA* **112**, 9158–9165 (2015).
159. Rosenhall, U., Johansson, E. & Gillberg, C. Oculomotor findings in autistic children. *J. Laryngol. Otol.* **102**, 435–439 (1988).
160. Takarae, Y., Minshew, N. J., Luna, B., Krisky, C. M. & Sweeney, J. A. Pursuit eye movement deficits in autism. *Brain* **127**, 2584–2594 (2004).
161. Takarae, Y., Minshew, N. J., Luna, B. & Sweeney, J. A. Oculomotor abnormalities parallel cerebellar histopathology in autism. *J. Neurol. Neurosurg. Psychiatry* **75**, 1359–1361 (2004).
162. Luna, B., Doll, S. K., Hegedus, S. J., Minshew, N. J. & Sweeney, J. A. Maturation of executive function in autism. *Biol. Psychiatry* **61**, 474–481 (2007).
163. De Rubeis, S. *et al.* Synaptic, transcriptional and chromatin genes disrupted in autism. *Nature* **515**, 209–215 (2014).
164. DeLorey, T. M. *et al.* Somatosensory and sensorimotor consequences associated with the heterozygous disruption of the autism candidate gene, *Gabrb3*. *Behav. Brain Res.* **216**, 36–45 (2011).
165. Banerjee, A. *et al.* Jointly reduced inhibition and excitation underlies circuit-wide changes in cortical processing in Rett syndrome. *Proc. Natl Acad. Sci. USA* **113**, E7287–E7296 (2016).
166. Selimbeyoglu, A. *et al.* Modulation of prefrontal cortex excitation/inhibition balance rescues social behavior in *CNTNAP2*-deficient mice. *Sci. Transl Med.* **9**, eaah6733 (2017).
167. Tabuchi, K. *et al.* A neuroligin-3 mutation implicated in autism increases inhibitory synaptic transmission in mice. *Science* **318**, 71–76 (2007).
168. McAlonan, G. M. *et al.* Brain anatomy and sensorimotor gating in Asperger's syndrome. *Brain* **125**, 1594–1606 (2002).
169. Madsen, G. F., Bilenberg, N., Cantio, C. & Oranje, B. Increased prepulse inhibition and sensitization of the startle reflex in autistic children. *Autism Res.* **7**, 94–103 (2014).
170. Kohl, S. *et al.* Prepulse inhibition of the acoustic startle reflex in high functioning autism. *PLoS ONE* **9**, e92372 (2014).
171. LeBlanc, J. J. *et al.* Visual evoked potentials detect cortical processing deficits in Rett syndrome. *Ann. Neurol.* **78**, 775–786 (2015).
172. Sutherland, A. & Crewther, D. P. Magnocellular visual evoked potential delay with high autism spectrum quotient yields a neural mechanism for altered perception. *Brain* **133**, 2089–2097 (2010).
173. Flevaris, A. V. & Murray, S. O. Orientation-specific surround suppression in the primary visual cortex varies as a function of autistic tendency. *Front. Hum. Neurosci.* **8**, 1–9 (2015).

174. Keehn, B. & Joseph, R. M. Exploring what's missing: what do target absent trials reveal about autism search superiority? *J. Autism Dev. Disord.* **46**, 1686–1698 (2016).
175. Mayer, J. L. The relationship between autistic traits and atypical sensory functioning in neurotypical and ASD adults: a spectrum approach. *J. Autism Dev. Disord.* **47**, 1–12 (2016).
176. Takayama, Y. *et al.* Standardization of the Japanese version of the Glasgow Sensory Questionnaire (GSQ). *Res. Autism Spectr. Disord.* **8**, 347–353 (2014).
177. Horder, J., Wilson, C. E., Mendez, M. A. & Murphy, D. G. Autistic traits and abnormal sensory experiences in adults. *J. Autism Dev. Disord.* **44**, 1461–1469 (2013).
178. Tavassoli, T., Hoekstra, R. A. & Baron-Cohen, S. The Sensory Perception Quotient (SPQ): development and validation of a new sensory questionnaire for adults with and without autism. *Mol. Autism* **5**, 29 (2014).
179. Ujiie, Y. & Wakabayashi, A. Psychometric properties and overlap of the GSQ and AQ among Japanese university students. *Int. J. Psychol. Stud.* **7**, 195–205 (2015).
180. Mottron, L. & Burack, J. A. in *The Development of Autism Perspectives from Theory and Research* (eds Burack, J. A., Charman, T., Yirmiya, N. & Zelazo, P. R.) 131–148 (Erlbaum, 2001).
181. Pellicano, E. & Burr, D. When the world becomes 'too real': a Bayesian explanation of autistic perception. *Trends Cogn. Sci.* **16**, 504–510 (2012).
182. Cermak, S. A. & Daunhauer, L. A. Sensory processing in the postinstitutionalized child. *Am. J. Occup. Ther.* **51**, 500–507 (1997).
183. Nelson, C. A. A. Neurobiological perspective on early human deprivation. *Child Dev. Perspect.* **1**, 13–18 (2007).
184. Bassili, J. N. Facial motion in the perception of faces and of emotional expression. *J. Exp. Psychol. Hum. Percept. Perform.* **4**, 373–379 (1978).
185. Crane, E. & Gross, M. in *Affective Computing and Intelligent Interaction* (eds Paiva, A. C. P., Prada, R. & Picard, R. W.) 95–101 (Springer Berlin Heidelberg, 2007).
186. Markram, H., Rinaldi, T. & Markram, K. The intense world syndrome — an alternative hypothesis for autism. *Front. Neurosci.* **1**, 77–96 (2007).
187. Brock, M. E. *et al.* Temperament and sensory features of children with autism. *J. Autism Dev. Disord.* **42**, 2271–2284 (2012).
188. Kuhl, P. K. & Meltzoff, A. N. The bimodal perception of speech in infancy. *Science* **218**, 1138–1141 (1982).
189. McGurk, H. & MacDonald, J. Hearing lips and seeing voices. *Nature* **264**, 746–748 (1976).
190. Tager-Flusberg, H. On the nature of linguistic functioning in early infantile autism. *J. Autism Dev. Disord.* **11**, 45–56 (1981).
191. Bedny, M., Pascual-Leone, A. & Saxe, R. R. Growing up blind does not change the neural bases of Theory of Mind. *Proc. Natl Acad. Sci. USA* **106**, 11312–11317 (2009).
192. Happé, F. & Frith, U. The weak coherence account: detail-focused cognitive style in autism spectrum disorders. *J. Autism Dev. Disord.* **36**, 5–25 (2006).
193. Mountcastle, V. B. The columnar organization of the neocortex. *Brain* **120**, 701–722 (1997).
194. Reynolds, J. H. & Heeger, D. J. The normalization model of attention. *Neuron* **61**, 168–185 (2009).
195. Lee, T. S. & Mumford, D. Hierarchical Bayesian inference in the visual cortex. *J. Opt. Soc. Am. A Opt. Image Sci. Vis.* **20**, 1434–1448 (2017).
196. Shipp, S., Adams, R. A. & Friston, K. J. Reflections on agranular architecture: predictive coding in the motor cortex. *Trends Neurosci.* **36**, 706–716 (2013).
197. Frank, M. C. & Goodman, N. D. Predicting pragmatic reasoning in language games. *Science* **336**, 998 (2012).
198. Koster-Hale, J. & Saxe, R. Theory of Mind: a neural prediction problem. *Neuron* **79**, 836–848 (2013).
199. Barrett, L. F. & Simmons, W. K. Interoceptive predictions in the brain. *Nat. Rev. Neurosci.* **16**, 419–429 (2015).
200. Brock, J. Alternative Bayesian accounts of autistic perception: comment on Pellicano and Burr. *Trends Cogn. Sci.* **16**, 573–574 (2012).
201. Van de Cruys, S., Van der Hallen, R. & Wagemans, J. Disentangling signal and noise in autism spectrum disorder. *Brain Cogn.* **112**, 78–83 (2016).
202. Haker, H., Schneebeli, M. & Stephan, K. E. Can Bayesian theories of autism spectrum disorder help improve clinical practice? *Front. Psychiatry* **7**, 107 (2016).
203. Lawson, R. P., Mathys, C. & Rees, G. Adults with autism overestimate the volatility of the sensory environment. **2017**, 4–6 (2017).
204. Frith, U. & Snowling, M. Reading for meaning and reading for sound in autistic and dyslexic children. *Br. J. Dev. Psychol.* **1**, 329–342 (1983).
205. D'Souza, D., Booth, R., Connolly, M., Happé, F. & Karmiloff-Smith, A. Rethinking the concepts of 'local or global processors': evidence from Williams syndrome, Down syndrome, and Autism Spectrum Disorders. *Dev. Sci.* **19**, 452–468 (2016).
206. Rayomnd, W. & Gibbs, Jr. A new look at literal meaning in understanding what is said and implicated. *J. Pragmat.* **34**, 457–486 (2002).
207. Desimone, R. & Duncan, J. Neural mechanisms of selective visual attention. *Annu. Rev. Neurosci.* **18**, 193–222 (1995).
208. Gopnik, A. & Rosati, A. Duck or rabbit? Reversing ambiguous figures and understanding ambiguous representations. *Dev. Sci.* **4**, 175–183 (2001).
209. Sobel, D. M., Capps, L. M., Gopnik, A., Capps, L. M. & Gopnik, A. Ambiguous figure perception and theory of mind understanding in children with autistic spectrum disorders. *Br. J. Dev. Psychol.* **23**, 159–174 (2005).
210. Doherty, M. J. & Wimmer, M. C. Children's understanding of ambiguous figures: which cognitive developments are necessary to experience reversal? *Cogn. Dev.* **20**, 407–421 (2005).
211. Rogers, S. J., Hepburn, S. & Wehner, E. Parent reports of sensory symptoms in toddlers with autism and those with other developmental disorders. *J. Autism Dev. Disord.* **33**, 631–642 (2003).
212. Kern, J. K. *et al.* The pattern of sensory processing abnormalities in autism. *Autism Int. J. Res. Pract.* **10**, 480–494 (2006).
213. Baranek, G. T. Autism during infancy: a retrospective video analysis of sensory-motor and social behaviors at 9–12 months of age. *J. Autism Dev. Disord.* **29**, 213–224 (1999).
214. Robertson, A. E. & Simmons, D. R. Sensory sensitivities in autism spectrum disorders: a qualitative analysis [Abstract]. *International Meeting for Autism Research* (2010).
This large-scale survey, now twice replicated, shows that trait measures of sensory sensitivities and social interaction difficulties co-vary in the general population.
215. Frazier, T. W. *et al.* Validation of proposed DSM-5 criteria for autism spectrum disorder. *J. Am. Acad. Child Adolesc. Psychiatry* **51**, 28–40.e3 (2012).
216. Goodbourn, P. T. *et al.* Variants in the 1q21 risk region are associated with a visual endophenotype of autism and schizophrenia. *Genes Brain Behav.* **13**, 144–151 (2014).
217. Goodbourn, P. T. *et al.* Cortical patterning genes are associated with individual differences in visual orientation perception. *Invest. Ophthalmol. Vis. Sci.* **55**, 6396 (2014).
218. Ausderau, K. K. *et al.* Sensory subtypes in children with autism spectrum disorder: latent profile transition analysis using a national survey of sensory features. *J. Child Psychol. Psychiatry.* **55**, 935–944 (2014).
219. Rogers, S. J. & Ozonoff, S. Annotation: what do we know about sensory dysfunction in autism? A critical review of the empirical evidence. *J. Child Psychol. Psychiatry.* **46**, 1255–1268 (2005).
220. Tetzchner, S. *et al.* Vision, cognition, and developmental characteristics of girls and women with Rett syndrome. *Dev. Med. Child Neurol.* **38**, 212–225 (1996).
221. Lee, S. H. *et al.* Genetic relationship between five psychiatric disorders estimated from genome-wide SNPs. *Nat. Genet.* **45**, 984–994 (2013).
222. Tibber, M. S. *et al.* Visual surround suppression in schizophrenia. *Front. Psychol.* **4**, 88 (2013).
223. Yoon, J. H. *et al.* Diminished orientation-specific surround suppression of visual processing in schizophrenia. **35**, 1078–1084 (2009).
224. Tadin, D. *et al.* Weakened center-surround interactions in visual motion processing in schizophrenia. *J. Neurosci.* **26**, 11403–11412 (2006).
225. Stanley, J., Park, S., Blake, R. & Carter, O. Binocular rivalry dynamics and mixed percept in schizophrenia. *Front. Hum. Neurosci.* http://dx.doi.org/10.3389/conf.fnhum.2015.217.00325 (2015).
226. Cornelissen, P., Richardson, A., Mason, A., Fowler, S. & Stein, J. Contrast sensitivity and coherent motion detection measured at photopic luminance levels in dyslexics and controls. *Vision Res.* **35**, 1483–1494 (1995).
227. Eden, G. F. *et al.* Abnormal processing of visual motion in dyslexia revealed by functional brain imaging. *Nature* **382**, 66–69 (1996).
228. Goswami, U. Sensory theories of developmental dyslexia: three challenges for research. *Nat. Rev. Neurosci.* **16**, 43–54 (2015).
229. Olulade, O. A., Napoliello, E. M. & Eden, G. F. Abnormal visual motion processing is not a cause of dyslexia. *Neuron* **79**, 180–190 (2013).
230. Sandin, S. *et al.* The familial risk of autism. *JAMA* **311**, 1770 (2014).
231. Hallmayer, J. *et al.* Genetic heritability and shared environmental factors among twin pairs with autism. *Arch. Gen. Psychiatry* **68**, 1095 (2011).
232. Ronemus, M., Iossifov, I., Levy, D. & Wigler, M. The role of *de novo* mutations in the genetics of autism spectrum disorders. *Nat. Rev. Genet.* **15**, 133–141 (2014).
233. Chen, J. A., Peñagarikano, O., Belgard, T. G., Swarup, V. & Geschwind, D. H. The emerging picture of autism spectrum disorder: genetics and pathology. *Annu. Rev. Pathol.* **10**, 111–144 (2015).
234. Moessner, R. *et al.* Contribution of *SHANK3* mutations to autism spectrum disorder. *Am. J. Hum. Genet.* **81**, 1289–1297 (2007).
235. Yi, F. *et al.* Autism-associated SHANK3 haploinsufficiency causes I_h channelopathy in human neurons. *Science* **352**, aaf2669 (2016).
236. Bourgeron, T. From the genetic architecture to synaptic plasticity in autism spectrum disorder. *Nat. Rev. Neurosci.* **16**, 551–563 (2015).
237. Silverman, J. L., Yang, M., Lord, C. & Crawley, J. N. Behavioural phenotyping assays for mouse models of autism. *Nat. Rev. Neurosci.* **11**, 490–502 (2010).
238. Happé, F., Ronald, A. & Plomin, R. Time to give up on a single explanation for autism. *Nat. Neurosci.* **9**, 1218–1220 (2006).
239. Ronald, A., Happé, F. & Plomin, R. The genetic relationship between individual differences in social and nonsocial behaviours characteristic of autism. **5**, 444–458 (2005).
240. Ronald, A. *et al.* Genetic heterogeneity between the three components of the autism spectrum: a twin study. *J. Am. Acad. Child Adolesc. Psychiatry* **45**, 691–699 (2006).
241. Robinson, E. B. *et al.* A multivariate twin study of autistic traits in 12-year-olds: testing the fractionable autism triad hypothesis. *Behav. Genet.* **42**, 245–255 (2012).
242. Frazier, T. W. *et al.* A twin study of heritable and shared environmental contributions to autism. *J. Autism Dev. Disord.* **44**, 2013–2025 (2014).
243. Lidstone, J. *et al.* Relations among restricted and repetitive behaviors, anxiety and sensory features in children with autism spectrum disorders. *Res. Autism Spectr. Disord.* **8**, 82–92 (2014).
244. Boyd, B. A., McBee, M., Holtzclaw, T., Baranek, G. T. & Bodfish, J. W. Relationships among repetitive behaviors, sensory features, and executive functions in high functioning autism. *Res. Autism Spectr. Disord.* **3**, 959–966 (2009).
245. Lynch, M. & Walsh, B. *Genetics and analysis of quantitative traits* (Sinauer, 1998).

Acknowledgements
The authors thank M. Cohen, A. Spiegel, G. Choi, N. Kanwisher, A. J. Haskins, and M. Sur for comments on sections of this manuscript and helpful discussion.

Author contributions
C.E.R. researched the article. C.E.R. and S.B.-C. equally contributed to discussions of the content, writing the article and to review and/or editing of the manuscript before submission.

Competing interests statement
The authors declare no competing interests.

Publisher's note
Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

SUPPLEMENTARY INFORMATION
See online article: S1 (box)
ALL LINKS ARE ACTIVE IN THE ONLINE PDF