Supplementary information S1 (box)

More information about whether visual processing of affective information is fast

The work on object perception briefly discussed in the main text builds upon earlier studies on scene perception[1] and 'ultra-rapid' visual perception. In particular, rapid perception may be linked to electrophysiological responses with latencies ~150 ms (ref.[2]). Advances in our understanding of rapid visual perception also stem from computational modeling work inspired by the organization of the visual system, which has revealed that feedforward architectures can account for the performance of humans in rapid categorization tasks[3, 4]. Several properties of these computational models match neuronal responses in monkey IT cortex[5] and responses in human temporal cortex (measured using electrocorticography) when viewpoint-invariant visual object categories are discriminated as early as 100 ms after presentation[6]. In other words, this theoretical work suggests that the feedforward machinery of the visual system is capable of complex computations in very short periods of time (such as generating viewpoint-invariant representations).

Another important aspect of the work on rapid visual perception concerns attention. There is evidence that visual perception of non-affective stimuli is not only fast, but also may require less attention than is often thought. For instance, the rapid visual categorization of novel natural scenes requires little focal attention[7], indicating that perception outside the focus of attention may extend beyond simple and salient stimuli (see also ref [8]). This work is relevant in the context of the standard hypothesis because it shows that many types of seemingly complex visual perceptions can take place even when processing resources are scarce – thus, not only emotional information enjoys this 'privileged status'.

More information about the processing of coarse and fine visual information

Vuilleumier et al. (ref [9]) reported that the fusiform gyrus, in contrast to the amygdala, is sensitive to high spatial-frequency (SF) information. Other studies, however, indicate that the fusiform gyrus is sensitive to both low- and high-SF information[10, 11]. These findings are of relevance in the context of the standard hypothesis because they raise the possibility that the origin of the enhanced amygdala responses to low-SF faces reported originally[9] may have been (at least in part) cortical, given that the signals in the fusiform gyrus would be expected to 'feed into' the amygdala (given the connectivity between anterior temporal cortex and the amygdala[12]).

More information about the pulvinar

Next to nothing is known about the connectivity and electrophysiology of the pulvinar in humans, although a diffusion tensor imaging study has reported results consistent with connectivity to ipsilateral SC as well as temporal visual cortices[13]. A recent study in epileptic patients examined evoked responses to electrical stimulation to map the functional connectivity of the medial pulvinar and suggested functional connections with visual cortex and the amygdaloid region[14]. However, given the limited resolution and other characteristics of both of these techniques, it is not possible to conclude the existence of anatomical connectivity with certainty. Nevertheless, it is usually assumed that the human pulvinar has much the same connectivity as that found in monkeys.

Both neuroimaging and lesion studies in humans strengthen the notion that the pulvinar is involved in attentional functions. Whereas early Positron Emission Tomography studies are consistent with a role of the pulvinar in visual attention[15, 16] —including attentional filtering in the presence of distractors and selective attention to stimulus features (e.g., shape, color) — the low spatial resolution of this technique precluded anatomically clear conclusions. However, more recent studies at higher resolution during fMRI at 3T are consistent with these earlier results – e.g., responses in the pulvinar were only observed during attended conditions, but not when the stimulus was unattended[17]. Lesion studies have shown deficits of attention in the visual field contralateral to the pulvinar lesion[18]. Importantly, the pulvinar on the right hemisphere has been identified as an important subcortical node associated with spatial neglect[19, 20]. It is thought that 'driving inputs' (as opposed to 'modulatory inputs') to the pulvinar originate in cortex[21, 22] (see also below). Thus, pulvinar responses may be closely aligned with awareness because of the contributions from cortex, which is thought to be important for conscious perception.

There are several differences between the ventral and dorsal 'domains' of the pulvinar. Highlighting these differences are the following additional facts[23]. There is a dual representation of occipital areas in the ventral domain, but nothing comparable in the dorsal domain. Furthermore, a site in the dorsal pulvinar may be connected with relatively distal regions of the brain, for instance, in parietal and frontal cortex – this is unlike the ventral pulvinar, whose connectivity is restricted to the occipito-temporal cortex. In fact, many extensive fronto-parietal cortical connections are mirrored by overlapping fields in the dorsal pulvinar[24, 25]. In other words, if regions in frontal and parietal cortex are interconnected in the cortex, their projection sites in the pulvinar will typically coincide (and the connections are bidirectional between pulvinar and cortex) – an organization that further exemplifies the "associational" potential of the dorsal pulvinar.

An additional issue that warrants discussion concerns the connections from the superior colliculus to the pulvinar. Visual signals from the retina are conveyed to the superficial layers of the SC and then to the inferior pulvinar (which is part of the ventral domain) (Figure 3). However, connections also seem to exist from the intermediate/deep (nonretinal) layers of the SC to the medial pulvinar (which is part of the dorsal domain). Could the intermediate/deep layers be sending input to the amygdala via the medial pulvinar? This scenario is problematic for the following reasons. Although for simplicity we treated the medial pulvinar as a unit, there is strong evidence that this nucleus is comprised of central/lateral and medial sub-units with substantially different connectional patterns (see Figure 10 of ref. [24]). Furthermore, whereas the medial subunit projects to the amygdala, it is the central/lateral subunit that receives substantial input from the SC. Again, it seems unlikely that a simple colliculo-pulvino-amygdalar pathway exists (we thank Alan Anticevic for bringing up this point). Even more critically, signals from the intermediate and deep layers of the SC are multimodal in nature and possibly linked to saccadic eye movements. Thus, they would not easily fit the role commonly assumed in the purported subcortical pathway of the standard hypothesis.

More information about the subcortical pathway in rodents

An important question concerning subcortical pathways in rats (or other species) is whether they are functional under normal conditions, that is, in animals with intact brains. A relevant clue as to whether a pathway is functional under normal conditions relates to when the lesion took place in a particular study[26]. If the damage takes place prior to conditioning, for instance, then it is possible that other pathways may take over (because during conditioning alternate routes may be recruited that are also able to support learning). Thus, in cases in which a lesion occurs prior to conditioning, pathways may be identified that are *capable* of mediating fear conditioning even if they are not normally used. On the other hand, if the behavioral deficit is observed in the case of a post-training lesion, this would indicate that the pathway is *normally* used to mediate the effect (because the pathway normally used was compromised by the lesion).

These considerations are of relevance in the context of the experiment by Shi and Davis[26], who investigated the role of visual pathways to the amygdala during fear conditioning. In their study, post-training lesions of the lateral posterior nucleus of the thalamus (LP; a structure that is related to the pulvinar) did not block fear conditioning when a visual CS was employed. Because the LP gives rise to subcortical inputs to the amygdala, the results indicate that this pathway is likely not critical in mediating visually based fear conditioning in normal animals (i.e., without a lesion). Instead, another pathway identified in their study, which connects the LP to the basolateral amygdala via anterior temporal cortex, was critical for transmitting emotion-laden visual information. For a related discussion of whether the auditory subcortical pathway to the amygdala is also the primary driver of affective information in intact animals that have undergone fear conditioning, see the study by Shi and Davis[26], too.

In summary, in the context of the standard hypothesis, lesion studies need to carefully differentiate between pathways that are sufficient to carry affective information from those that are indeed functional in intact animals.

More information about multiple visual pathways and coarse information processing

The magnocellular system conveys low SF and motion information[27]. Bypass systems involving magnocellular projections are thus of interest as they may be especially fast. For instance, MT and FEF cells exhibit latencies 10-40 ms lower than V2 and V4 (ref [28]), consistent with non-hierarchical modes of communication. Anatomical studies have identified a direct LGN to MT pathway that may convey visual signals to MT in primates[29], together with a pathway to MT from the SC via the inferior pulvinar[30]. The latter pathway is particularly intriguing as it involves the two structures of the subcortical pathway of the standard hypothesis. Functional (as opposed to structural) identification of a colliculo-pulvino-MT pathway has been recently established by a combination of microstimulation and histological analysis[31]. The electroanatomical findings of this study provide evidence for the existence of at least two relay zones that ascend from the SC to MT through the inferior pulvinar.

Bypass systems have been investigated in humans, too. Functional evidence for the role of bypass systems in the cortex was reported in a recent case study[32] of a patient with developmental agnosia and prosopagnosia (with no discernible macroscopic cortical lesion). In this patient, V1 was robustly activated by visual stimuli (as measured with fMRI), but intermediate areas V2-V4 failed to be visually activated. Yet, robust 'downstream' activation was observed in the parahippocampal gyrus and other regions, with spared selectivity for houses and places. Bypass pathways have also been identified in patient GY[33] (who has been reported to exhibit affective blindsight[34]). Based on diffusion-weighted MRI, a pathway was detected that linked the right LGN to left MT, a pathway that was absent in control participants.

More information about the role of the amygdala in processing of affective information

If the amygdala is not responsible for non-conscious processing of emotional visual stimuli, what brain structures are? Although the issue of non-conscious processing is a complex and largely unresolved one[35], non-conscious processing of affective information, if present, may take place in a manner that is analogous to that for non-emotional information. For instance, long-range interactions involving the parietal and frontal cortex may be important in establishing sufficiently strong representations to support awareness[36, 37]. This, of course, does not exclude some role for the amygdala, but such role would be more modulatory than indispensable, not unlike its function during conscious processing.

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