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#### Research Focus Response

## Response to Small: Crossmodal integration – insights from the chemical senses

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A central prediction arising from studies of multisensory integration states that crossmodal binding should enhance measures of behavior, especially when a stimulus in one modality is degraded or ambiguous [1]. Of the human senses, olfaction is among the more underdetermined [2,3]. It thus follows that there should be substantial benefits to olfactory perception in the presence of relevant sensory cues in other modalities. In a recent study of olfactory–visual integration [4], we showed behavioral evidence for such an effect. Subjects detected an odor more quickly and more accurately when it was paired with a semantically congruent (versus incongruent) picture. Using functional magnetic resonance imaging (fMRI) techniques, we simultaneously characterized the neural substrates accompanying this behavioral facilitation. Our key finding was of enhanced activity in rostromedial orbitofrontal cortex (OFC), anterior hippocampus, intraparietal sulcus (IPS) and superior temporal sulcus (STS).

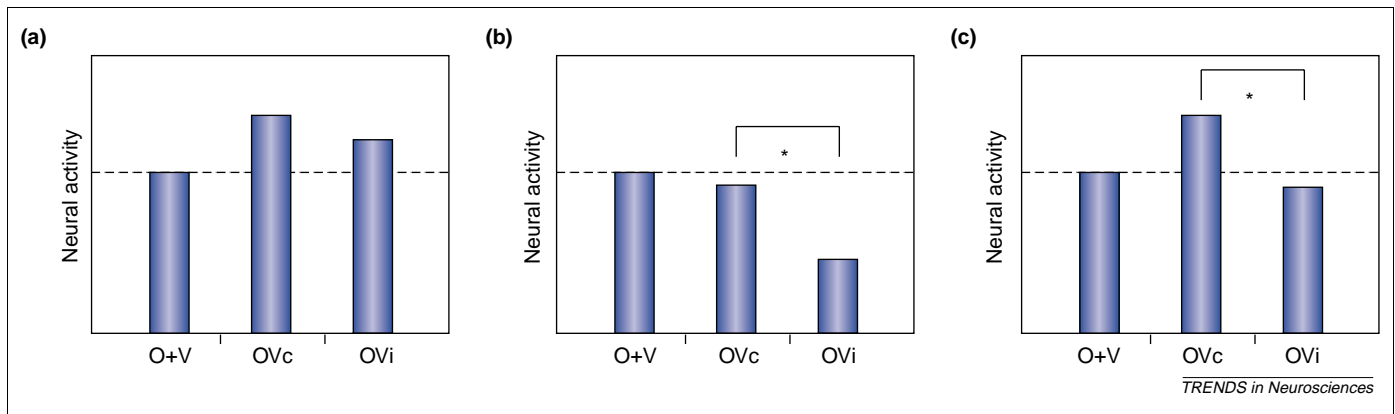
In an insightful commentary [5], Dana Small has placed our findings in the broader context of crossmodal integration and emphasized important distinctions between the chemical senses and other sensory domains of vision, audition and somatosensation. She has also extended the conceptual framework of Calvert [6] by suggesting that crossmodal enhancement of object identification in STS can be generalized to olfactory stimuli. Here, we provide a complementary perspective, to show how a focus on

response pattern differences can elucidate the functional roles of regions subserving olfactory–visual integration.

In our study, the first of these response patterns was identified in the formal interaction between odors and pictures. This analysis tested for bimodal responses exceeding the sum of unimodal constituents, a profile that corresponds to the responses of multisensory neurons in animal models [1]. Importantly, the approach makes no assumption about the degree of semantic relatedness between crossmodal stimuli. Indeed, animal and human studies indicate that temporal synchrony of unimodal inputs is sufficient to elicit multisensory integration [7–11]. This concept is exemplified in Figure 1a, which shows that supra-additive bimodal activity can occur irrespective of semantic congruency. In IPS, we detected neural responses of this general form. For visual, auditory and tactile modalities, IPS appears to facilitate processes such as crossmodal localization and spatial attention [6,12], and we suggest that IPS could play a similar role in the olfactory domain.

A second response pattern was demonstrated when we compared bimodal congruent and incongruent conditions. This analysis makes no assumption about whether areas sensitive to semantic effects also exhibit supra-additive multisensory interactions. It is plausible that regions tuned to semantic attributes might differ from those involved in crossmodal integration, or simply might not respond in a supra-additive manner. Thus, Figure 1b

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**Figure 1.** Different response patterns of olfactory–visual integration. **(a)** Multisensory supra-additivity. Bimodal olfactory–visual congruent (OVc) and bimodal olfactory–visual incongruent (OVi) responses both exceed the mere sum of unimodal olfactory and visual responses (O + V; dashed line). There is no significant difference between OVc and OVi, suggesting that this region is insensitive to shared semantic attributes. **(b)** Semantic congruency effect. The response to OVc is significantly higher than that to OVi (asterisk). However, the odor–picture interaction (supra-additive effect) is not significant, because neither bimodal item exceeds the unimodal sum. **(c)** Congruency-specific supra-additivity. The OVc response is greater than both the unimodal sum and the OVi response (which itself does not surpass the summed unimodal response).

depicts the activity pattern of a region sensitive to semantic congruency in the absence of multisensory supra-additivity. In our study, this profile was typified by responses elicited in anterior hippocampus. One interpretation of this finding is that the hippocampus mediates retrieval or reactivation of semantic associations between olfactory and visual stimuli, consistent with associative or relational models of hippocampal function [13,14].

Finally, we note that multisensory supra-additivity and semantic effects might not be mutually exclusive. Figure 1c depicts the activity pattern of a region sensitive to both components. Responses of this type were identified in OFC, and to a lesser extent in STS, whereby bimodal congruent activity was greater than the unimodal sum and greater than bimodal incongruent activity. In other words, the crossmodal interaction of odors and pictures was evident in rostral OFC and STS only when the unimodal constituents were semantically concordant. As discussed by Small [5], these cortical regions could participate more directly in odor identification.

The results described here indicate that basic principles of crossmodal integration are preserved across structures and across modalities. The demonstration of supra-additive response patterns in IPS and STS suggests that heteromodal sites long classified in non-olfactory terms also mediate crossmodal processing involving chemosensory stimuli. Areas of rostral OFC (and STS) display supra-additive profiles, preferentially to semantically congruent odor–picture pairs. By contrast, regions such as anterior hippocampus depart from this multisensory profile and respond primarily to the degree of shared semantic concordance between stimuli. We agree with Small's speculation [5] that hippocampus could be an intermediary in olfactory–visual integration, by using semantic information to sculpt OFC and STS activity and thereby disambiguate odor perception.

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