Synaesthesia: supernormal integration?

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Synaesthesia has been known to scientific research for over 100 years but has undergone something of a renaissance recently as new investigations begin to uncover its neurological basis. Rather than being an anomaly, it might offer beneficial insights into the basis of normal perception. A new study by Esterman *et al.* epitomises this current trend and claims to show that the posterior parietal cortex is a crucial locus of synaesthetic experience. As the posterior parietal cortex is commonly linked to normal sensory integration, Esterman *et al.*'s finding might lend support to the claim that synaesthesia is an extension of the normal perceptual processes assumed to occur in binding.

Synaesthesia occurs when an individual experiences sensations of attributes triggered reliably by specific external stimuli but not normally associated with those stimuli. It ranges in vividness and can occur between different senses, for example the sound of notes can trigger tastes or shapes. However it commonly occurs within a sense, for example, reading letters, words or numbers may trigger the sensation of colours [1]. Synaesthesia affects about 4% of the population [2], and understanding it requires the wider principles of cortical development, sensory organization, sensory integration and the generation of qualia to be addressed. A new study by Esterman *et al.* [3] marks an important step in understanding the neural basis of synaesthesia, and also speaks to these wider issues.

In recent years the efforts to understand the sensory cross-activation in synaesthesia have paralleled broader neuroscientific trends. For example, the identification of functionally specialized modules in the brain has been followed by a realization that understanding the interaction between modules in an extended network is as valuable as fractionating that network into its component parts [4]. Moreover, it is possible that different sensory mechanisms use common algorithms [5] that underpin cross-modal associations and synaesthesia; indeed, it might make them inevitable.

Esterman *et al.* address the idea that synaesthesia represents one end of a spectrum of sensory connectivity and focus on the role of the posterior parietal cortex in the synaesthetic process. Their study reflects a growing recognition that synaesthesia presents a means to investigate variability in modularity and interconnection between human sensory systems. In normal cross-modal integration, the ability to combine multiple sources of information yields the best estimate of the external properties of a stimulus [4], and reduces perceptual uncertainty [6]. It is therefore important to investigate whether synaesthetes' bimodal experiences (word–colour, tone–colour, smell–touch, etc.) are an extension of normal cross-modal integration [7].

Do synaesthetes bind?

Esterman *et al.* adapted the Stroop task (Figure 1) and presented two grapheme–colour synaesthetes with letters, which elicited a synaesthetic colour, and symbols, which did not. The letters were presented in a colour that was either congruent or incongruent with the synaesthetic colour normally triggered by that letter. Response time for identifying the physical colour of the letter was measured. A significant delay in naming incongruently coloured letters has been demonstrated in synaesthetes [8], and is used to indicate the presence and interference of synaesthetic colours.

In their experiment Esterman *et al.* applied repetitive Transcranial Magnetic Stimulation (rTMS) to the left and right angular gyri at the junction of the posterior intraparietal and transverse occipital sulci (IPS/TOS), and also to V1 as a control site. rTMS (480 pulses at 1 Hz for 8 min) was applied immediately before two blocks of 120 trials, counterbalanced with sham TMS. An increase in response latency would demonstrate interference with the synaesthetic process. Indeed, with sham TMS the synaesthetes displayed their usual response latency but after rTMS over

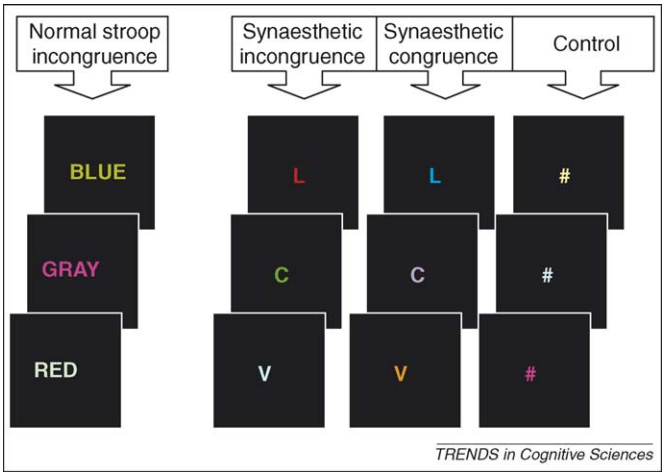

Figure 1. Adapting the Stroop task for synaesthesia. The Stroop Effect [10] describes the delay in reaction time when naming the ink colour of an incongruent colour-name (e.g. **blue**).This can be adapted for grapheme–colour synaesthesia [8]. When presented with a grapheme printed in a colour that is incongruent with its synaesthetic colour (e.g. printed in **red** when it triggers a synaesthetic **blue**) synaesthetes have a significant reaction-time delay in identifying the ink colour, which is not present for congruent (printed in **green** when it triggers a synaesthetic **green**) or control conditions (symbols that do not trigger a synaesthetic colour).

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the right IPS/TOS latencies were significantly slower. The authors concluded that: (i) feature binding of form and synaesthetic colour occurs at IPS/TOS, as in normal sensory binding; (ii) they have illuminated one of several mechanisms responsible for synaesthesia; and (iii) they support 'the theory that feedback from a multimodal association region, like the parietal cortex, contributes to the perception of a synaesthetic photism'.

Does this binding idea hold together?

The evidence is certainly intriguing. A previously overlooked pattern of parietal activation during synaesthetic experiences that was reported in several earlier fMRI investigations has recently been noted (e.g [9]). Here, Esterman *et al.* do indeed demonstrate the necessity of the posterior parietal lobe in synaesthetic colour interference; however, there might still be room for other interpretations.

It is not stated whether the synaesthetes experienced their synaesthetic colour on the trials on which they did not show interference. This could clarify whether the TMS interfered with the synaesthetic process *per se* or with some other component of the Stroop task, which has previously been associated with the PPC [10]. Esterman *et al.* discuss whether parietal TMS attenuates perceptual/conceptual conflict rather than binding. They argue against this on the grounds that traditional Stroop conflict survives bilateral TMS of, or lesions to, the parietal lobes. However, these tasks might not be directly comparable, because of the difference between conflict of externally presented perceptual and conceptual stimuli (traditional Stroop), and conflict of externally presented perceptual colour with the internally generated colours (synaesthetic Stroop). Esterman *et al.* also note PPC activity in three fMRI studies of synaesthesia that did not involve Stroop conflict. However, these studies presented graphemes in black which, although not incongruently chromatic, nonetheless pose a level of potential conflict between presented and synaesthetic colour.

Existing synaesthesia models

It remains debatable whether synaesthesia occurs as the result of atypical connections, such as between a colour-sensitive and a grapheme-sensitive region [11], or is an atypical use of normal perceptual mechanisms [12,13], such as disinhibition of feedback connections from multisensory areas (Figure 2). In the absence of direct measures of connectivity, neither theory has prevailed. Esterman *et al.*'s study is therefore particularly noteworthy in providing evidence of involvement of multimodal cortex, supporting the theory of an atypical use of normal perceptual mechanisms.

As synaesthesia is a heterogeneous phenomenon, caution should be taken when generalizing across synaesthetes. The two synaesthetes in this experiment represent a narrow sample of the synaesthetic spectrum; they report perceiving graphemes in synaesthetic colours. Other synaesthetes have reported experiencing diffuse patches of colour separate from the grapheme, or a black letter with a coloured background, or 'just knowing' the grapheme's colour without perceiving it [11]. It is an untested assumption that normal binding mechanisms would be as good a fit to these other kinds of synaesthetes. Esterman *et al.* suggest that parietal involvement might vary from synaesthete to synaesthete. If this is so, we are still left in search of a common route of the atypical connectivity that leads to the synaesthetic activation.

The absence of an effect of TMS applied over V1 requires further investigation, because some investigators argue that V1 is important in word–colour synaesthesia [14]. TMS over V1 stimulates part of a retinotopic map and it is therefore important to establish whether the visual stimuli presented were retinotopically aligned with the location of phosphenes. It remains possible that doing so could yield a positive finding.

In the context of other synaesthesia experiments, Esterman *et al.*'s study stands out both anatomically and methodologically. fMRI studies have shown that during the synaesthetic experience, automatic co-activation occurs

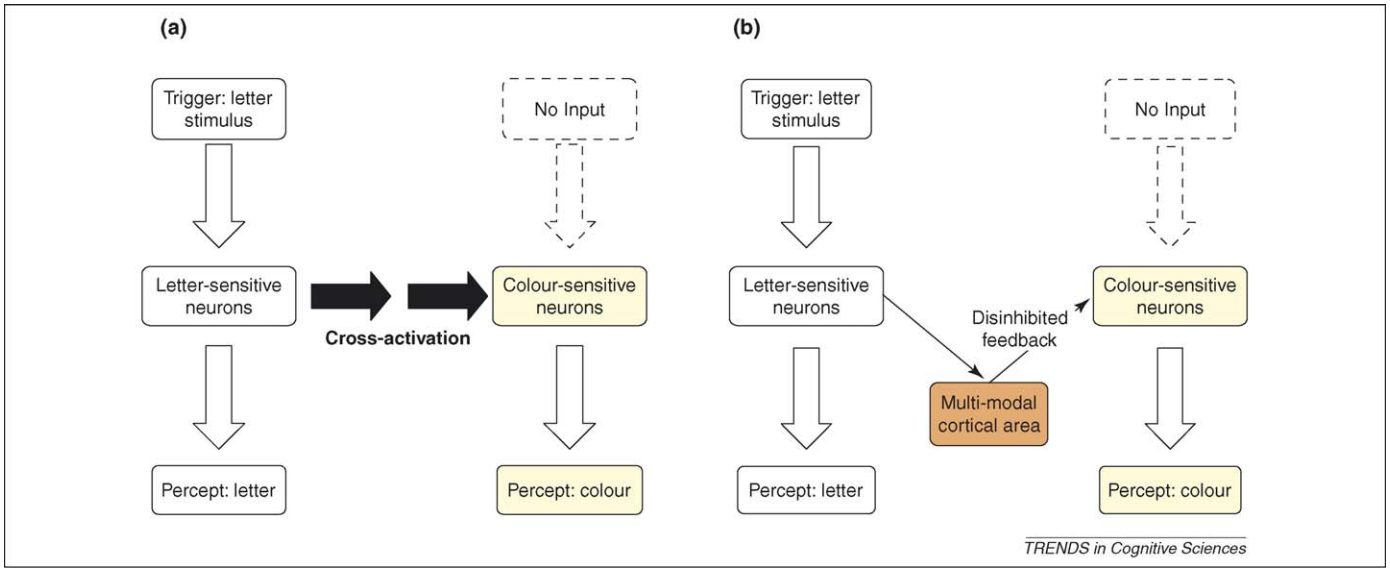

Figure 2. Two current theories of the basis of synaesthesia. It is not known how synaesthetic sensations are instantiated in the brain. Theories include **(a)** excess direct connections between neurons sensitive to the trigger stimulus and neurons sensitive to the secondary percept [11], and **(b)** disinhibition of normal connections to and from multimodal areas [13].

in brain areas usually associated with both the trigger sensation and the secondary sensation. For example, activation in left colour-sensitive cortex occurred in word–colour synaesthetes hearing words [14] but not in non-synaesthetes trained to associate colour with words [15]. Many issues concerning the anatomy underlying information processing in synaesthesia remain to be elucidated but this method of using interference techniques to investigate whether synaesthesia involves the same sensory multimodal areas that support cross-modal integration in non-synaesthetes is an important approach. The two immediate questions that pose themselves are how Esterman *et al.*'s finding will generalize to other synaesthetes and whether the timing of the putative synaesthetic binding is similar to that of sensory integration in non-synaesthetes.

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Letters

Improving reverse neuroimaging inference: cognitive domain versus cognitive complexity

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In a recent TICS article, Poldrack [1] offers a highly informative analysis of the use and misuse of 'reverse inference' in neuroimaging, a common practice by which the engagement of a particular cognitive process is inferred from the activation of a particular brain region. Using a formal Bayesian analysis framework, Poldrack shows that the usefulness of reverse inference depends on the selectivity of activation in the region of interest (the ratio of process-specific activation to the overall likelihood of activation in that region across all tasks). However, it is important to note that the usefulness of reverse inference also depends on whether the relevant task characteristics for the region of interest are taken into account.

Cognitive domain

Perhaps the most salient task characteristic is a task's cognitive domain. For example, distinctions are often made between attention, language and working-memory tasks. Some regions appear to show selectivity with respect to such domains. For example, Broca's area [Brodmann area (BA) 44] is more likely to be activated by language than by non-language tasks [1]. Other regions, however, such as the rostrolateral prefrontal cortex (RLPFC; lateral portion of BA 10), appear to have much lower domain-selectivity. Thus, activations in the RLPFC have been observed with similar probability across tasks in the domains of reasoning, working memory and episodic memory [2], as well as attention [3]. This lack of domain-specificity is not surprising, given that the functions of this region probably include highly integrative, abstract cognitive processes [2,4,5]. If tasks that recruit this region were defined solely in terms of their cognitive domain, this lack of selectivity would seem to preclude reverse neuroimaging inference altogether.

Cognitive complexity

On the other hand, if such tasks were defined in terms of their level of cognitive complexity, selectivity of RLPFC activation would be relatively high. Cognitive complexity

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