PHILOSOPHY

EVIDENCE AGAINST FUNCTIONALISM FROM NEUROIMAGING OF THE ALIEN COLOUR EFFECT IN SYNAESTHESIA

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ABSTRACT

Coloured hearing synaesthetes experience colours to heard words, as confirmed by reliability of self-report, psychophysical testing and functional neuroimaging data. Some also describe the 'alien colour effect' (ACE): in response to colour names, they experience colours different from those named. We have previously reported that the ACE slows colour naming in a Stroop task, reflecting cognitive interference from synaesthetically induced colours, which depends upon their being consciously experienced. It has been proposed that the hippocampus mediates such consciously experienced conflict. Consistent with this hypothesis, we now report that, in functional magnetic resonance imaging of the Stroop task, hippocampal activation differentiates synaesthetes with the ACE from those without it and from non-synaesthete controls. These findings confirm the reality of coloured hearing synaesthesia and the ACE, phenomena which pose major challenges to the dominant contemporary account of mental states, functionalism. Reductive functionalism identifies types of mental states with causal roles: relations to inputs, outputs and other states. However, conscious mental states, such as experiences of colour, are distinguished by their qualitative properties or *qualia*. If functionalism is applied to conscious mental states, it identifies the qualitative type of an experience with its causal role or function. This entails both that experiences with disparate qualitative properties cannot have the same functional properties, and that experiences with disparate functional properties cannot have the same qualitative properties. Challenges to functionalism have often denied the first entailment. Here, we challenge the second entailment on empirical grounds. In coloured hearing synaesthesia, colour qualia are associated with both hearing words and seeing surfaces; and, in the ACE, these two functions act in opposition to one another. Whatever its merits as an account of other mental states, reductive functionalism cannot be the correct account of conscious experiences.

Key words: synaesthesia, alien colour effect, functionalism, Stroop effect, hippocampus, conflict

INTRODUCTION

The dominant contemporary theory of how mental states are related to brain-and-behaviour is *functionalism* (Dennett, 1991; for discussion see McGinn, 1982; Block, 1980; Chalmers, 1996; Shear, 1998; Gray, 2004). There are many varieties of functionalism. Their common element, however, is the understanding of types of mental states in terms of their causal or functional role – their sensory inputs, behavioural outputs and relations to other types of mental states – as opposed to in terms of the physical substance that underlies that functional role - such as living neural tissue (McGinn, 1982; Block 1980a; Chalmers, 1996). The more ambitious, general and reductive forms of functionalism (Chalmers, 1996) that are our concern here identify functional roles with types of mental state (for discussion, see Block and Fodor, 1980; Clark, 1998)[1].

Some conscious mental states, such as experiences of colour, are distinguished by their qualitative properties or *qualia* (for this usage see, e.g., Shoemaker, 1980; Churchland, 2002). If reductive functionalism is applied to conscious mental states, it identifies the qualitative type of an experience with its causal role or function; *qualia* as such are held to have no independent properties that determine their nature. This entails both (a) that experiences with disparate qualitative properties cannot have the same functional properties, and (b) that experiences with disparate functional properties cannot have the same qualitative properties[2]. So the following questions

†Jeffrey Gray, first author of this article, died during the final preparation of this manuscript.
A long term supporter of Synaesthesia research, he held the fervent belief that within the Synaesthete lay a key to the understanding of how Brain and Mind are connected – a meeting point for Neuroscience and Neurophilosophy.
These, his final recorded thoughts on the matter, are dedicated to his memory.

[1]When we speak of "functionalism" here, we intend reductive functionalism, though we will not continually repeat this qualification. Nonreductive functionalism holds only that functional role *determines* type of mental state (Chalmers, 1996, 1998), rather than *identifying* functional role with type of mental state. This means that the type of mental state cannot vary independently of functional role; mental type in some way arises from or supervenes on functional role, even if not identified with it.

[2]If nonreductive functionalism is applied to conscious mental states, it holds that the qualitative type of an experience is determined by but not identified with its causal role or function, which entails (a) but not (b).

would all be given the same general answer by reductive functionalists:

1) What makes colour experiences different from experiences of smell?

2) What makes the experience of a shape different from the experience of high C played on a violin?

3) What makes the experience of red different from the experience of green?

4) What makes the experience of a red afterimage have the same colour qualia as the experience of a red apple?

For each qualitative type of experience, the functionalist points to its sensory inputs from and behavioural outputs to the environment plus its relations to other mental states understood in terms of information processing, but typically ignoring the role played in this processing by brain tissue as such. Having thus set out the different functional roles of each qualitative type of experience, the reductive functionalist believes that he has given a complete answer to each of these questions.

Conscious mental states with qualia are often regarded as problematic for functionalism (McGinn, 1982; Shoemaker, 1980; Block, 1980b; Tye, 1996; Chalmers, 1996, 1998). Challenges to functionalism based on qualia have often denied entailment (a), for example by asserting the metaphysical possibility of qualia inversion whereby the quality of the perceptual experience of, say, the colour red for one subject is identical to the quality of the perceptual experience of, say, the colour green for another subject, although in terms of behaviour, the responses of the two subjects are the same. In what follows, we challenge reductive functionalism on empirical grounds by denying entailment (b).

Reductive functionalism has until recently been treated mainly as a philosophical rather than an empirical claim (there are early exceptions, e.g., Cole, 1990). It leads, however, to empirical predictions. Of particular concern here is the prediction that experiences with two different functional roles should not have the same qualia, since if they do, the qualitative type of an experience cannot be identified with its functional role. Coloured hearing synaesthesia apparently contradicts this prediction, since synaesthetes report that seeing coloured surfaces and hearing spoken words each give rise to qualia of identical colour-type, although this is not to say that the two are indistinguishable in other respects (Gray et al., 2002). It helps to make the argument clearer if one keeps in mind that qualia are qualitative properties that apply to sets of conscious experiences; they are not individual conscious experiences. Normal people rarely have difficulty in distinguishing whether a subjective experience has the qualitative property, for example, of colour, seen motion, smell, touch, etc. They are confident that they do *not* experience stimuli presented in the auditory modality as having color qualia. Coloured hearing synaesthetes, in contrast, have experiences with colour qualia in response to heard words. They know that these experiences have colour qualia because they have the same kind of qualia as do experiences elicited by visually perceived coloured surfaces, which are also described by non-synaesthetes as experiences of colour. Such synaesthetes are indeed able to distinguish their colour experiences elicited through the auditory and visual channels, respectively, but they are in no doubt that both have colour qualia. Since reductive functionalism identifies the subjective qualitative properties of a given set of experiences with the functional roles these experiences standardly have (for that is how functionalism accounts for the difference between auditory and visual qualia), the counter-instance offered to reductive functionalism by coloured hearing synaesthesia is clear: different role, same qualitative property – a direct challenge to entailment (b) (but see Noë and Hurley, 2003; Gray, 2004; Hurley and Noë, 2005 for alternative views). There need not be further evidence of complete identity between all the subjective qualitative properties of the experiences elicited by the visual and auditory routes in synaesthesia. That would be tantamount to claiming that the redness of an after-image is necessarily different from the redness of a seen object because the subject can distinguish the one from the other.

Given the conceptual importance of coloured hearing synaesthesia, it has been important to validate experimentally the self-reports of synaesthetes. This has been achieved by showing reliability of self-report of the synaesthetic colours evoked by words over a one-year interval (Baron-Cohen et al., 1993), perceptual pop-out of 'coloured graphemes' (black-against-white numerals seen by the synaesthete as coloured; Ramachandran and Hubbard, 2001) and activation in functional magnetic resonance imaging (fMRI) of colour-relevant regions of the visual system in synaesthetes, but not controls, presented with spoken words (Nunn et al., 2002). One class of synaesthetic self-report for which neurobiological validation is, at present, lacking is the alien colour effect (ACE). ACE coloured hearing synaesthetes report that, in response to colour names, they experience colours different from those named (Gray, 1999). This phenomenon is critical for reductive functionalism, for two reasons. First, if synaesthesia were due to associative learning, it would not pose a challenge to functionalism. Synaesthesia arising in this way would be no more difficult to explain in functionalist terms than other idiosyncratic consequences of specific learning experiences, e.g., aversion to the taste of water-melon (Dickinson, 2001). However, on this associative learning account, there should be no ACE, as any initial incongruent word-colour associations should undergo reversal learning on the repeated everyday occasions when colour names are followed by correct colours. Yet, like other synaesthetic experiences, the adult synaesthete describes the ACE as having been present

since early childhood. Second, the self-reported ACE is associated with slowed colour naming (Gray et al., 2002). Thus, in this condition not only are two functional roles (hearing words and seeing colours) linked to the same qualia but, *in virtue of this very linkage*, the two functions actively interfere with one another.

Slowed colour naming in coloured hearing synaesthetes who report the ACE (Gray et al., 2002) resembles the 'Stroop' effect observed in normal subjects (McLeod and MacDonald, 2000). In a standard Stroop task the subject names the 'ink' colour either of a control stimulus (e.g., a row of Xs) or of an incongruent colour name (e.g., the word 'red' presented in green ink). Naming of the incongruent colour name is slower; this is the 'Stroop effect'. Slowed colour naming associated with the ACE presumably arises in a similar fashion: when the subject retrieves the name of the ink colour, this evokes an incongruent synaesthetic colour which interferes with uttering the correct colour name (Gray et al., 2002). The two forms of interference are additive. We observed equal slowing of colour naming relative to non-synaesthete controls when synaesthetes with the ACE were required to name the ink colour of either rows of Xs or incongruent colour names; and the standard exteroceptive Stroop effect did not differ between the synaesthetes and controls (Gray et al., 2002).

We here used functional magnetic resonance imaging (fMRI) to seek neurobiological confirmation of the reality of the ACE. While we were uncertain of whether ACE and non-ACE synaesthetes would differ in terms of activation to seen colour surfaces or heard coloured words, for the Stroop task we predicted differences in brain activity between the ACE and control groups, either within the neural system activated by the Stroop task itself, or outside it, through the recruitment of additional brain regions. Consistent with this prediction, we demonstrate differences in blood-oxygen-level-dependent (BOLD) activity during a standard Stroop task in coloured hearing synaesthetes with the ACE relative to both non-synaesthetes and coloured hearing synaesthetes without the ACE.

Materials and Methods

Subjects

Right-handed female synaesthetes, recruited from our data base, reporting coloured hearing with (n = 8) or without (n = 7) the ACE (Gray, 1999; Gray et al., 2002) and non-synaesthete controls (n = 8) were matched ($F < 1$ for differences between groups) on the National Adult Reading Test (Nelson and Willison, 1991) [ACE synaesthetes, mean 121.50 ± (SD) 2.98; non-ACE synaesthetes, 117.71 ± 6.37; controls, 119.75 ± 3.41] and age (ACE synaesthetes, mean 52.25 years, range 23-78; non-ACE synaesthetes, 47.29, 41-68; controls, 42.50, 28-54). The behavioural data in Experiment 3 were lost for one control subject. In Experiments 1 and 2 fMRI data were not collected for some subjects or discarded due to excessive movement artefact (see legend to Figure 1 for reduced group sizes). All synaesthetes (and no control) reported seeing colours in response to heard words but not to other auditory stimuli. Coloured hearing synaesthesia was confirmed by a test of genuineness (Baron-Cohen et al., 1993), i.e. reliability of self-reported colour experiences evoked by a list of words over a one-year test-retest interval. Experiments 1 and 2 assessed the comparability of the synaesthetes studied here and by Nunn et al. (2002). The percentage of colour names subject to the ACE (i.e., eliciting experienced colours different from the colour named; Gray et al., 2002) was zero for all non-ACE synaesthetes and 60-100% in the ACE synaesthetes. No subject had a history of neurological or psychiatric disease or was taking psychoactive drugs. All subjects gave informed consent and the study was approved by the Institute of Psychiatry Research Ethics committee.

Procedures

In a single 1-h fMRI session, subjects participated in three experiments, each employing a "box-car" design to contrast an experimental with a control condition: in Experiment 1, words *versus* tones; in Experiment 2, coloured *versus* monochrome "Mondrian" patterns; in Experiment 3 (the main experiment), Stroop (colour names presented in incongruent colours) vs. control (coloured rows of Xs or colour patches). Experiments 1 and 2 were identical to Experiments 1 and 3 reported in Nunn et al., (2002). In Experiment 3 stimuli were projected onto a screen placed across the bore of the MR magnet, 1.8 m from the subjects' eyes, and viewed through an angled mirror. In the Stroop condition, the stimuli were the words blue, green, yellow and red, printed in blue, green, yellow and red "ink". Congruent pairings (e.g., the word 'blue' printed in blue ink) were excluded. We used two control conditions, one (Steel et al., 2001) in which a row of 3-6 Xs was displayed, again in blue, green, yellow or red ink, and a second (Gruber et al., 2002) consisting of patches of the same colours. This was done to control for the possibility that the rows of Xs might, as verbal stimuli, elicit colour experiences in the synaesthetes. Approximately equal numbers of subjects were tested using each of the two control conditions. Although naming speed was slower overall for rows of Xs (736.66 ± 151.55 msec) than colour patches (541.00 ± 107.07 msec, $t_{20} = 3.56$, $p < .002$), this variable did not interact with synaesthesia or the ACE, and its inclusion did

not alter any of the results reported. It will therefore not be considered further. Subjects were instructed to whisper into a microphone, as quickly as possible, the name of the ink colour of each stimulus with minimal head or lip movement. Reaction times (RT), recorded by voice key, were measured from stimulus onset to the naming response. The first RT in each block was excluded in the analysis, as were RTs where an error had been made. Each stimulus had a presentation time of 2.5 sec and consisted of a fixation cross, displayed for 500 msec, followed by the stimulus (word, Xs or colour patch) for 100 msec, and then a blank screen for 1900 msec. The experiment lasted 5 min, comprising 10 × 30 sec blocks (each of 8 stimuli), to which the Stroop and control conditions were allocated in a quasi-random order fixed across subjects. Subjects first carried out two practice trials of the Stroop condition.

Image Acquisition and Analysis

Image acquisition, data pre-processing (to minimise motion artefacts) and modelling of experimentally-induced haemodynamic responses (using linear combinations of Poisson functions) were carried out as described in detail previously (Nunn et al., 2002). These processes yielded a goodness of fit statistic (ratio of model to residual sum of squares – SSQ ratio) for each individual at each voxel upon which inferential analysis (identification of activated voxels) could be performed, using null distributions computed by wavelet-based time series resampling techniques (Bullmore et al., 2001). Group activation maps for ACE, non-ACE and non-synaesthetes were constructed by transforming the SSQ ratio maps computed from the observed and wavelet-resampled data for each individual into the standard stereotactic space of Talairach and Tournoux (1988). Significant group activations, robust to outlier effects, were identified by comparing the group median SSQ ratio in the observed data at each voxel with appropriate critical values in the null distribution of median SSQ ratios computed from the spatially transformed wavelet resampled data (Bullmore et al., 2001). In order to enhance sensitivity of detection and take into account neighbourhood relationships between activations, we used a method of cluster analysis described previously and validated extensively (Bullmore et al., 1999). Simulations using false activations embedded in null data obtained using the same image acquisition parameters have shown that BOLD effects as small as .2-.3% of the mean image intensity levels can be detected reliably if these activations are consistent across groups of at least 6 individuals. These findings warrant confidence that negative findings (e.g., here, the lack of hippocampal activation by the Stroop condition in the non-synaesthete group; Table I) are not simply ascribable to lack of sensitivity of the fMRI analysis. Qualitative comparisons between ACE, non-ACE and non-synaesthete groups were made by visual inspection of the group activation maps. Quantitative comparisons were made in separate ANOVA models for each group pairing (ACE *vs.* non-ACE, ACE *vs.* non-synaesthete, non-ACE *vs.* non-synaesthete).

TABLE I

Stroop-specific activations (Stroop minus control condition) in non-synaesthetes (Experiment 3). Statistical thresholds are as described in the legend to Figure 2. All activations are in the left hemisphere.

Brain region	Talairach coordinates		
	x	y	z
Superior temporal gyrus	– 51	4	4
	– 32	– 48	20
	– 47	– 15	– 13
	– 43	– 15	– 18
Medial temporal gyrus	– 36	– 4	– 7
	– 29	– 56	15
Superior parietal lobe	– 36	– 59	48
Inferior parietal lobe	– 36	– 56	42
	– 43	– 52	31
Precuneus	– 25	– 59	37
	– 22	– 70	48
Inferior frontal gyrus	– 43	11	15
Cuneus	– 22	– 78	31
	– 29	– 74	37
Medial occipital gyrus	– 25	– 81	20
Insula	– 36	0	– 2
Claustrum	– 32	– 15	9

RESULTS

Experiment 1 (Figure 1A) confirmed our previous findings (Nunn et al., 2002). Inspection of the group maps shows that, in coloured hearing synaesthetes with and without the ACE but not non-synaesthetes, spoken words activate a posterior, ventrolateral region of temporal cortex in the left hemisphere. The qualitative similarity between left ventrolateral temporal activity in ACE and non-ACE synaesthetes was confirmed by quantitative statistical testing, no significant difference being found in response amplitude within the region. In Experiment 2 (Figure 1B) non-synaesthetes showed, as expected (Bartels and Zeki, 2000), bilateral activation of V4 in response to coloured Mondrians. As in previous studies (e.g., Zeki et al., 1991), there was a degree of asymmetry with more voxels active in left than right V4. Confirming our previous findings (Nunn et al., 2002), in the non-ACE synaesthetes coloured Mondrians activated V4 predominantly in the right hemisphere. This difference in laterality of V4 response between non-synaesthetes and non-ACE synaesthetes was confirmed by statistical test, non-synaesthetes having a significantly greater amplitude ($p < .001$) left-sided V4 activation to colour than non-ACE synaesthetes. In contrast, coloured Mondrians

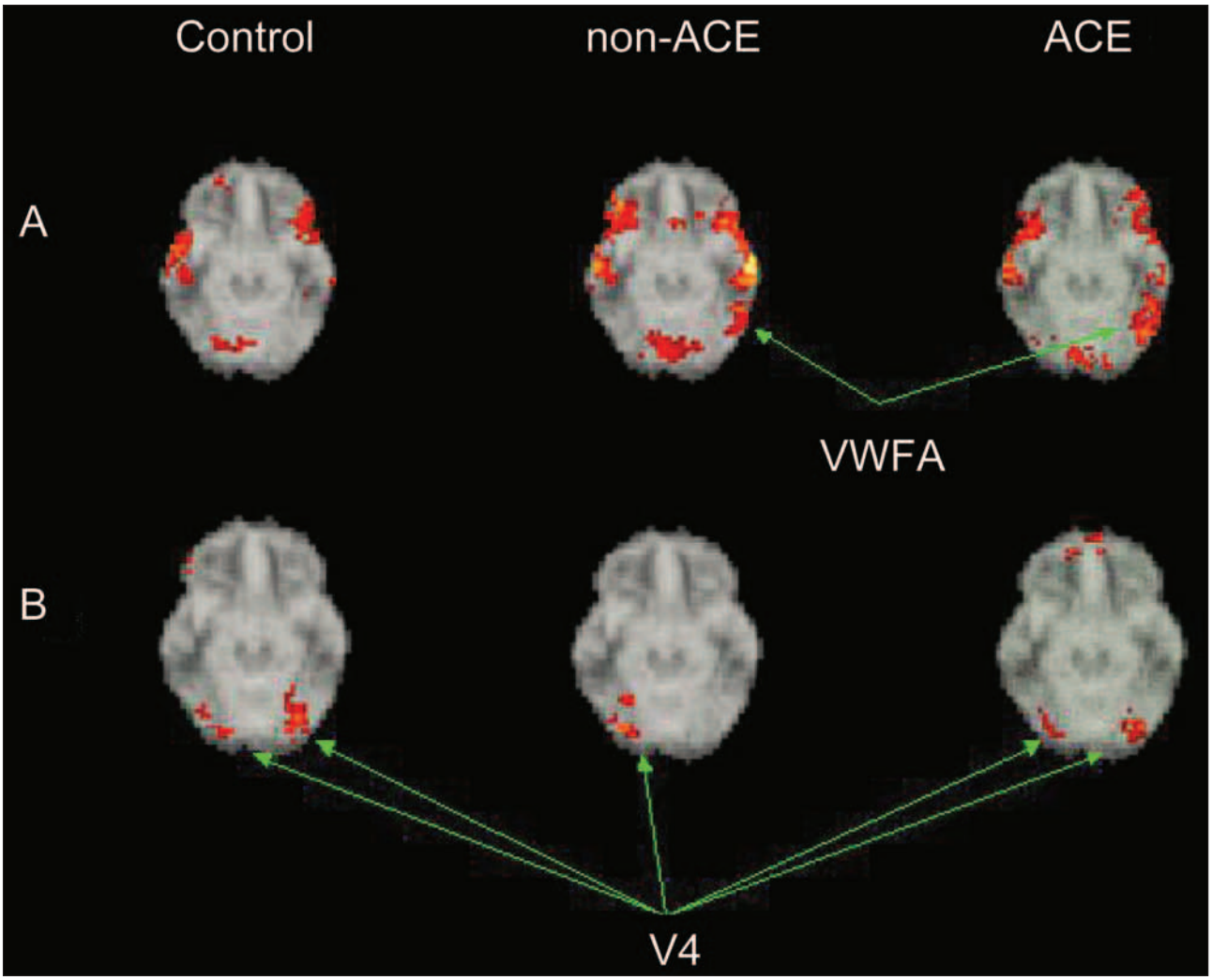

Fig. 1 – *Results of Experiments 1 (A: words minus tones) and 2 (B: coloured minus monochrome Mondrians). Cluster level activation maps are shown for non-synaesthete controls (left) and for synaesthetes with (right) and without (central) the alien colour effect (ACE). For words minus tones, the analysis revealed activations within the Visual Word Form Area (VWFA) (Cohen et al., 2000) in the non-ACE synaesthetes (n = 6; – 51, – 44, – 13 [peak co-ordinate]) and in the ACE synaesthetes (n = 8; – 43, – 63, – 13), but not in the controls (n = 5). For coloured minus monochrome Mondrians, the analysis revealed activations bilaterally within V4 in controls (n = 7; Left – 29, – 70, – 13; Right 36, – 67, – 13) and ACE synaesthetes (n = 8; Left – 32, – 74, – 13; Right 29, – 78, – 13), but only in right V4 in the non-ACE synaesthetes (n = 5; 26, – 64, – 7). All data shown are at Talairach z plane – 13 (the peak co-ordinate in the non-ACE synaesthetes was found at z = – 7, but the – 13 slice is shown for consistency). The cluster level statistical analysis was performed at a type I error rate of p = .0375 voxel-wise and p = .001 cluster-wise. At these thresholds, less than one false positive cluster is expected in the intracerebral volume tested. In order to show the relative power of response at each voxel a colour code indicating the voxel-wise type I error probability has been used. This runs from red (p = .0375) through to yellow (p = .00005). Data have been superimposed on a high-resolution volumetric image mapped into Talairach space. The left side of each image corresponds to the right hemisphere.*

activated V4 bilaterally in ACE synaesthetes, the bilateral activity showing the same left hemispheric predominance as found in non-synaesthetes. The qualitative difference in laterality between ACE and non-ACE synaesthetes was not found to be significant on quantitative statistical testing, an apparent inconsistency that may simply reflect a deficiency in the statistical power of our group comparison test (see Discussion).

The main experiment set relatively undemanding conditions for the Stroop task, omitting the negative priming condition employed by Gray et al. (2002), thus providing a baseline against which additional interference due to the ACE might be more readily detectable in fMRI. Accuracy of colour naming was near-perfect (< 1% errors) in all groups, compared to c. 10% errors in our previous purely behavioural study (Gray et al., 2002). Similarly, reaction times (RTs) were c. 100 msec slower and about equal, in the present control condition, to those in the Gray et al. (2002) Stroop condition. Probably for this reason, the groups did not differ in overall speed of colour naming ($F < 1$), in contrast to our previous finding that the ACE slows colour naming (Gray et al., 2002). Mean RTs were for the control condition 621.05 msec ± (SD) 158.10, and Stroop condition 791.04 ± 174.31. This Stroop effect, $F(1, 19) = 90.23$, $p < .001$, as in our previous study (Gray et al., 2002), did not interact with Group ($p = .10$).

Consistent with task demands for cross-mapping between vision and language, the areas

TABLE II

Regions of differential stroop-specific activation or Stroop-specific suppression between ACE synaesthete and non-ACE synaesthete or non-synaesthete groups. Statistical thresholds are as described in the legend to Figure 2.

			ACE *vs*. non-ACE Talairach			ACE *vs*. non-synaesthete Talairach		
Brain region			x	y	z	x	y	z
Differential activations								
ACE > control groups	Supplementary motor area	L	– 4	– 15	59	– 4	– 11	59
	Hippocampus	R	40	– 15	– 18	29	– 44	– 2
			32	– 19	– 13			
			36	– 37	– 7			
Control groups > ACE	Dorsal precuneus	R	7	– 56	– 48	7	– 63	48
Differential suppressions								
ACE > control groups	N/A	–	–	–	–	–	–	–
Control groups > ACE	Posterior cingulate	L	– 7	– 59	9	– 7	– 56	9
			– 4	– 59	– 15	– 7	– 59	15
						– 7	– 44	26
		R	4	– 48	26			
			7	– 44	31			
	Ventral precuneus	R	14	– 59	40	0	– 74	42

activated in non-synaesthetes in the Stroop *minus* control comparison (Table I) included left-lateralised regions concerned with visual (cuneus, medial occipital gyrus), auditory language (superior and medial temporal gyrus, inferior frontal gyrus; Gaillard et al., 2003) and cross-modal (claustrum; Olson et al., 2002) processing. Stroop-related activation in the precuneus (Banich et al., 2000; Steel et al., 2001; Fan et al., 2003) and insula (Steel et al., 2001) confirms previous findings. Posterior parietal activation (Brodmann areas 7, 40) has been observed (Zahn et al., 2000) in relation to semantic processing, required here to disambiguate the correct colour name. We did not see activation in the cingulate cortex, probably due to the ease of our task as cingulate activation in the Stroop task is inversely related to performance accuracy (Gruber et al., 2002). As in previous studies of the Stroop effect (Banich et al., 2000; Steel et al., 2001; Fan et al., 2003), there was no activation in the hippocampus.

The main experimental hypothesis – that the ACE would lead to differences in brain activity during the Stroop task compared to control groups – was tested by quantitative statistical comparison of Stroop-specific responses (i.e., Stroop *minus* control condition) in ACE, non-ACE and non-synaesthete groups. We also investigated the possibility that the three groups would differ in their Stroop-specific patterns of suppression (i.e., control condition *minus* Stroop). We report here only those consistent patterns of activation or suppression present when the ACE synaesthetes were compared to *both* the non-ACE synaesthete *and* the non-synaesthete groups (Table II). The ACE synaesthetes showed greater Stroop-specific activation in the supplementary motor area and in the right hippocampus. The latter activation affected the full extent of the hippocampus in the comparison with non-ACE synaesthetes, following the contours of hippocampal anatomy across four axial slices (Figure 2). In the equivalent comparison with non-synaesthetes, the increase in activity for the ACE was restricted to the posterior part of the hippocampus and the parahippocampal gyrus. Conversely, in the dorsal precuneus both the non-synaesthetes and non-ACE synaesthetes showed greater Stroop-specific activation than the ACE synaesthetes. Finally, ACE synaesthetes showed less Stroop-specific suppression in the posterior cingulate and ventral precuneus. No brain regions were more suppressed by the Stroop task in the ACE group than the non-ACE or non-synaesthete groups.

Discussion

The ACE and coloured hearing in general depend initially for their identification upon the self-report of the synaesthete. Despite the unusual, even seemingly bizarre, nature of these self-reports, our results show that they predict the results of empirical studies. Thus, we have demonstrated the reliability of the observation (Nunn et al., 2002), now repeated four times, that spoken words activate a left posterior, ventrolateral region of temporal cortex in coloured hearing synaesthetes. While the co-ordinates of this activity in our previous study (Nunn et al., 2002) overlapped those of V4 and neighbouring V4a (Bartels and Zeki, 2000), the foci observed here were located more laterally, corresponding better to the recently characterised (Cohen et al., 2000) visual word form area (VWFA; Figure 1A) specialised for visual representations of words and letter strings. It is unclear whether this difference between our two studies reflects inter-subject variability in the neurobiology of synaesthesia or our previous (Nunn et al., 2002) focus on areas of overlap between synaesthetic and

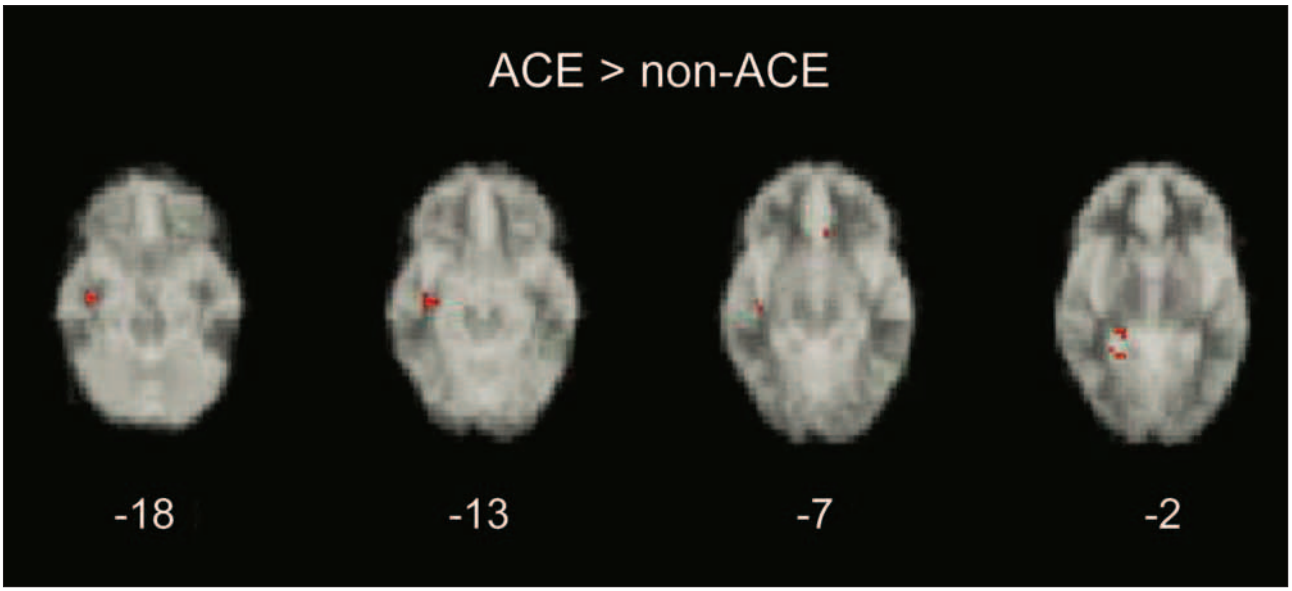

Fig. 2 – *Results of Experiment 3: Stroop-specific (i.e., Stroop minus control condition) patterns of activation in the ACE compared to non-ACE synaesthetes. Each image displays, at the Talairach z coordinate shown beneath it, greater ($p < .001$) right hippocampal activation in the ACE than non-ACE synaesthetes. The left side of each image corresponds to the right hemisphere.*

Mondrian colour activations. The latter is more likely, as activity centred on V4/V4a in our previous study also extended into the VWFA. Furthermore, at a cortical level, colour, letter-string, face and object specialisations of the ventral temporal lobe are organised as a patch-like mosaic (with a tendency of like-specialised patches to cluster together) rather than strictly segregated regions (Puce et al., 1999). The distinction between colour and letter-string specialised cortex may thus be less absolute than is suggested by differences in imaging co-ordinates. In either case, our results are consistent with the hypothesis that coloured hearing synaesthesia results from an extra aberrant projection from left-sided cortical language areas to left temporal regions specialised for colour (V4/V4a) and/or word forms (VWFA), and that the consequent activation of these regions by auditory language stimuli is sufficient to cause the conscious experience of colour (Ramachandran and Hubbard, 2001; Gray et al., 2002; Nunn et al., 2002).

Our results confirm in the group of synaesthetes without the ACE our previous report (Nunn et al., 2002) that, in subjects with coloured hearing, coloured Mondrians activate only right-sided V4, although this was not the result obtained in the synaesthetes with the ACE where activity was similar to that found in non-synaesthetes with bilateral V4 activity, more prominent on the left. Rigorous statistical comparison failed to find a significant difference in V4 activation between the two synaesthete groups, making the qualitative group laterality difference difficult to interpret. A lack of statistical significance may simply reflect a large inter-subject response variability which, for the relatively small number of subjects tested, limits statistical power to detect true group differences. Since we were able to detect differences between non-synaesthete and non-ACE groups, the problem does not seem to be a general lack of sensitivity in the statistical method employed, but rather one of response variability in the ACE group. Assuming the qualitative difference in V4 laterality between ACE and non-ACE synaesthetes to be real (but below the threshold of statistical significance), its interpretation is further hampered by our lack of understanding of such colour activation asymmetries in non-synaesthetes. The early reports (Zeki et al., 1991) of a normal left V4 predominance for full field colour stimuli, replicated here in the non-synaesthete and ACE groups, remain unexplained. Further studies are required to resolve this issue.

Our main aim was to determine whether the self-reported ACE is associated with differential activity during a Stroop task. This was the case, as supported by comparisons of Stroop-specific activity patterns in coloured hearing ACE synaesthetes with those in non-synaesthetes and, most stringently, synaesthetes who share coloured hearing but lack the ACE. Several brain regions were found differentially activated or suppressed in the two comparisons including the hippocampus, parahippocampal gyrus, dorsal and ventral precuneus, posterior cingulate gyrus and supplementary motor area. We will consider the implications of each of these differential activities in turn.

Hippocampus

Although the two major contemporary theories of hippocampal function attribute to this structure roles in spatial cognition (O'Keefe and Nadel, 1978) or episodic memory (Squire, 1992), without further

elaboration these two theories cannot both be correct. A third theory helps unify the two by proposing a more general function of the hippocampus in resolving goal conflict (Gray, 1995; Gray and McNaughton, 2000), from which are derived specific roles in spatial cognition, episodic memory and anxiety (Gray, 1982; Ploghaus et al., 2001). Our finding of increased Stroop-specific hippocampal activity in ACE compared to both control groups would seem to support this third theory as neither spatial cognition nor episodic memory are likely to play a significant role in the Stroop effect, the ACE or their combination. In contrast, an increase in hippocampal activity in the ACE is entirely predicted by the third theory, as the combination of interference from the Stroop task and the ACE would place heavy demands on the process of goal conflict resolution. This Stroop-specific hippocampal activation in the ACE contrasts with its absence in non-synaesthetes, here as in other studies of the Stroop effect (Banich et al., 2000; Steel et al., 2001; Fan et al., 2003). Interestingly, the role of the hippocampus in episodic memory (Maguire et al., 2001) or, more generally, in goal conflict is thought to be especially relevant for experiences that are conscious (Gray, 1995; Gray and McNaughton, 2000). The Stroop-related hippocampal activation in the ACE thus provides evidence of a specific behavioural/neurobiological effect related to the conscious nature of the synaesthetic experience. This mirrors the Mattingley et al. (2001) finding that interference from synaesthetic colours occurs only when those colours are experienced consciously, contrasting with standard Stroop interference which persists when the interfering stimulus is presented below the threshold of conscious awareness.

Precuneus, Posterior Cingulate and Parahippocampal Gyrus

Several regions concerned with *inter alia* visual imagery and visuo-spatial processing exhibited Stroop-specific activation or suppression differences between the ACE synaesthete and control groups. Some of these regions (e.g., precuneus) have been identified in previous Stroop studies (Banich et al., 2000; Steel et al., 2001; Fan et al., 2003). Taken together, the differential activations and suppressions imply that ACE synaesthetes were using visual imagery and visuo-spatial strategies more than non-ACE or non-synaesthete groups for some aspects of the task and less than non-ACE or non-synaesthete groups for other aspects. How these differences in strategy relate to the phenomenological experience of the ACE is unclear.

Supplementary Motor Area

Activation of the supplementary motor area is thought to relate to the need to inhibit prepotent responses (Rubia et al., 2001). Thus activation of this area in the ACE synaesthetes is likely to reflect the additional requirement in these subjects to inhibit utterance of the name of the synaesthetically experienced colour.

Neurobiological and Neurophilosophical Implications

Interpretation of our imaging results is uncomplicated by behavioural differences between the groups in either overall speed of colour naming or the Stroop effect itself. The failure of the ACE to affect colour naming, in contrast to the previously observed slowed RTs (Gray et al., 2002), probably reflects the relative ease of our task, as shown both behaviourally (near-perfect accuracy and slow overall RTs) and by the absence of Stroop-related cingulate activation, a neurobiological marker of Stroop task difficulty (Gruber et al., 2002). The lack of difference between synaesthetes, with or without the ACE, and controls on the exteroceptive Stroop effect confirms our previous findings (Gray et al., 2002). Consistent with the behavioural independence of the two effects (Gray et al., 2002), activation related to the ACE largely affected regions, especially the hippocampus, not implicated in the Stroop effect itself. We see this activation as reflecting, not the neurobiological basis of synaesthesia or the ACE as such, but rather a secondary consequence of the conflict engendered by the latter.

Our findings provide substantial neurobiological support for the reality of the ACE. This phenomenon is incompatible with accounts of coloured hearing synaesthesia in terms of early associative learning, as such associations would not survive the repeated occasions for reversal learning entailed by the ACE (Gray et al., 2002; Gray, 2004). The most likely alternative is an extra, genetically-determined, anatomical pathway linking the inducing and induced stimulus modalities at cortical level, i.e., linking language cortex to VWFA and/or V4 (Ramachandran and Hubbard 2001; Gray et al., 2002; Nunn et al., 2002). 'Hard-wired' linkage in this way of two disparate functions (processing, respectively, surface reflectance and speech) to a common qualitative property (colour) is incompatible (Gray et al., 2002) with the dominant contemporary account of mental states, functionalism, as applied to conscious mental states with qualitative properties. It is no defence against this critique that the closest neural correlate (NCC) (Crick and Koch, 1998) of veridical colour experience (V4) is not necessarily identical to the NCC for synaesthetic colour experience (in the present experiment, the VWFA: compare Figures 1A and B). Functionalism is indifferent to the nature of the stuff (which need not even be biological) that discharges functions. It is physicalism (Block, 1997), not functionalism, which holds that the same qualia should be

accompanied by the same neural activity. Our data suggest that, in coloured hearing synaesthetes, a qualitative color property may occur in association *both* with two disparate functions (contrary to functionalism) *and* with activity in two separate brain areas (contrary to phyicalism).

Equally incompatible with functionalism is the linkage, in coloured hearing synaesthetes with the ACE, between a functional role and conscious experiences that adversely compete with it (Gray et al., 2002). This conflict is confirmed here by its associated neural activation, especially in the hippocampus. To the extent that functionalism purports to provide a completely general account of how behavioural and brain processes relate to conscious experience, the negative instances afforded by coloured hearing synaesthesia and the ACE may be sufficient to dethrone it (Gray et al., 2002).

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