

To appear in
Visual Perception - Fundamentals of Awareness: Multi-Sensory Integration and High-Order Perception
(Editors: Martinez-Conde, S., Macknik, S.L., Martinez, L.M., Alonso, J-M., & Tse, P.U.).
Progress in Brain Research, Vol. 155, pp 263-275. London: Elsevier Science.
ISBN: 0444519270

Cross-Modal Interactions: Lessons from Synesthesia

Noam Sagiv* and Jamie Ward

Department of Psychology, University College London

* Present address: Centre for Cognition & Neuroimaging, Brunel University, Uxbridge, UB8 3PH, United Kingdom <http://people.brunel.ac.uk/~hsstnns/>

Keywords:

Synesthesia, Synaesthesia, Number-Forms, Crossmodal Perception, Multisensory Integration, Anomalous Experience.

ABSTRACT:

Synesthesia is a condition in which stimulation in one modality also gives rise to a perceptual experience in a second modality. In two recent studies we found that the condition is more common than previously reported; up to 5% of the population may experience at least one type of synesthesia. Although the condition has been traditionally viewed as an anomaly (e.g., breakdown in modularity), it seems that at least some of the mechanisms underlying synesthesia do reflect universal cross-modal mechanisms. We review here a number of examples of cross-modal correspondences found in both synesthetes and non-synesthetes including pitch-lightness and vision-touch interaction, as well as cross-domain spatial-numeric interactions. Additionally, we discuss the common role of spatial attention in binding shape and color surface features (whether ordinary or synesthetic color). Consistently with behavioral and neuroimaging data showing that chromatic-graphemic (colored-letter) synesthesia is a genuine perceptual phenomenon implicating extrastriate cortex, we also present electrophysiological data showing modulation of visual evoked potentials by synesthetic color congruency.

Introduction

Narrowly defined, synesthesia is a condition in which stimulation in one sensory modality evokes an additional perceptual experience in another modality. For example, sounds may evoke colors for some individuals (e.g., Ginsberg, 1923). While various sensory combinations have been described (e.g., Day, 2004, Cytowic, 2002), a common type of synesthesia in which seen letters and numbers induce color experience actually occurs intramodally in vision (e.g., Ramachandran & Hubbard, 2001a). Furthermore, it is clear that the meaning of the inducing stimulus is implicated in synesthesia at least sometimes rather than its lower level physical features (Myles et al., 2003). Moreover, certain concepts (e.g., days of the week) may induce synesthesia when synesthetes are thinking about them, hearing about them, or reading about them. Ordinal sequences (e.g., letters, numbers, and time units) often serve as inducers. In the recent literature, these have been regarded as variants of synesthesia. Nevertheless, it is still a matter of some debate how inclusive the definition of synesthesia should be. For example, there is no consensus concerning synesthesia-like cross-domain phenomena involving spatial forms or personification (e.g., Calkins, 1895). We do not use the term synesthesia to describe any cross-modal correspondences and associations, but rather only those cases in which a perceptual experience is involved, i.e., what Martino and Marks (2001) call *strong synesthesia*.

Synesthesia exists in developmental and acquired forms. The former runs in the family (e.g., Baron-Cohen et al, 1996; Ward & Simner, 2005) while the latter has been described in a variety of conditions as well as altered states of consciousness. Some examples include synesthesia following brain or nerve injury (Jacobs et al., 1981), synesthesia in late-blind individuals (Armel & Ramchandran, 1997; Steven & Blakemore, 2004). Hallucinogens such as LSD, mescaline (Hartman & Hollister, 1963) or ayahuasca (Shanon, 2002) often induce synesthetic hallucination. It is also reported by healthy individuals between sleep and wakefulness (Sagiv & Ben-Tal, in preparation) and a high proportion of meditators (Walsh, 2005).

Developmental synesthesia is thought to be characterized by a remarkable consistency of synesthetic correspondence within an individual across time (which has, in fact, been used as one diagnostic criterion). Still, synesthetes rarely agree on particular synesthetic correspondence (see for example Pat Duffy and Carol Steen's colored alphabets; Duffy, 2001) However, some trends can be traced in large synesthete populations (e.g., Shanon, 1982; Day, 2004; Rich et al, 2005). Beyond disagreement on particular correspondences, substantial heterogeneity is often found in phenomenological description, for example, in the spatial extent of synesthetic percepts (e.g., Dixon et al, 2004; Sagiv, 2004). Indeed we are only beginning to appreciate individual difference among synesthetes currently grouped together under single labels (Dixon & Smilek, 2005; Hubbard et al., 2005).

Synesthesia is involuntary and automatically evoked (in contrast to imagery at will). It is unclear whether similar underlying mechanisms give rise to developmental and acquired synesthesia. Reports of acquired synesthesia are largely anecdotal; however, it is possible that some predisposition is required. Additionally, positive symptoms are often under-reported, however, and thus prevalence of acquired synesthesia is harder to establish. Similarly, individuals with developmental synesthesia may have not realized that how they perceive the world is unusual in any way.

It has been suggested that synesthesia is unidirectional (Mills et al., 1999). Phenomenologically, this seems to be the case (e.g., pain may evoke a bright orange color, however, orange objects do not usually induce pain). However, at least in numerical

cognition, evidence for bi-directional interaction between color and magnitude processing is available (Cohen-Kadosh et al., 2005; Knoch et al., 2005).

Prevalence

Estimate concerning the prevalence of (developmental) synesthesia vary widely. Early surveys, relying on subjective reports, suggested that up to 1 in 5 individuals may have some form of synesthesia (e.g., Uhlich, 1957). Estimates based on self-referred samples have been far more pessimistic. Cytowic (1997) estimated that only 1 in 25000 may experience the condition, while Baron-Cohen et al (1996) estimated that the condition is present in *at least* 1 in 2000 individuals. Baron-Cohen and his colleagues combined for the first time subjective reports with an objective test of genuineness (testing for consistency synesthetic correspondences) thus ensuring low rate of false-alarms. However, because the prevalence estimate was based on the number of people responding to a newspaper advertisement (divided by readership figures), many cases were probably missed either because they did not see the ad, or saw it but chose not to respond.

The best estimate we have so far comes from two large scale surveys we recently conducted (Simner et al., in press). In both we combined objective and subjective methods for ascertaining synesthesia, but minimized self-referral bias. One survey in London's Science Museum included 1190 unsuspecting visitors. The study was conducted in an interactive gallery in the museum, and visitor cooperation was high, although they did not know what the purpose of the experiment was. Here we looked at chromatic-graphemic synesthesia (the most common type in self-referred samples). Participants were requested to choose a color that 'goes best' with letters and numbers. The process was repeated immediately, yielding a measure of consistency. Following this participants were asked direct questions concerning synesthetic experience. (1.1%) of the individuals tested were identified as chromatic-graphemic synesthetes.

In the second survey of multiple types of synesthesia among 500 Scottish students who were given more information on the varieties of synesthesia, we identified 23 synesthetes (4.6%) of which about half only reported colored weekdays. The prevalence of chromatic-graphemic synesthesia in this sample (1.4%) was similar to that obtained in the museum study. In sum, the condition may not be so unusual and appears to be almost 2 orders of magnitude more common than previously regarded.

Indeed, some view synesthesia, not as an anomalous phenomenon, but rather as one reflecting a normal mode of cognition (for a discussion, see Sagiv, 2004) that remains implicit in most individuals. Consistent with this view is the high prevalence of synesthesia in a number of altered states of consciousness suggesting that many of us have some predisposition to synesthesia. In the next section we explore the idea that synesthesia shares much in common with normal perception and discuss some common mechanism and processes.

What does synesthesia share in common with normal perception?

All contemporary accounts of synesthesia propose that there is some anomalous connectivity or cross-activation between different regions of the brain. Aside from this broad consensus¹ there is disagreement about: the nature of the connectivity between regions (e.g. horizontal versus feedback connections); whether or not the pathways implicated in synesthesia are present in the normal population or whether synesthetes have some privileged pathways; and differences in how anomalous connectivity could be instantiated at the neural

¹ But c.f. Shanon (2003).

level (e.g. literal increases in white matter connections, or neurochemical differences). At present, nothing is known about possible structural differences between the brains of synesthetes and other members of the population (at either a micro- or macro- scale). As such, the processes underlying synesthesia have tended to be inferred from studies at a functional (e.g. fMRI) or cognitive level. For example, Nunn et al. (2002), reported V4/V8 activation induced by synesthetic color in synesthetes listening to spoken words (eyes closed). Behavioral evidence demonstrating that synesthesia could influence perception of the evoking stimulus (e.g., grouping, detection, and apparent motion) also strongly suggest that visual synesthetic experience taps into existing visual mechanisms (Ramachandran and Hubbard, 2001, Smilek et al., 2001; Blake et al., 2004).

In the remainder of this chapter, we will consider the extent to which synesthesia may utilize some of the same mechanisms found in other members of the population in situations of cross-modal perception. For example, it is generally accepted that there are cross-modal mechanisms for linking together sight and touch (e.g. Spence, 2002) and sight and sound (e.g., King & Calvert, 2001) when both modalities are stimulated. But could these same mechanisms be implicated in synesthetic experiences of touch given a unimodal visual stimulus, or synesthetic experiences of vision given a unimodal auditory stimulus?

Sound-Vision Synesthesia

According to a large self-referred sample of synesthetes, at least 18% of them experience color induced by auditory stimuli such as music and noise (Day, 2004). Many more synesthetes experience colors from speech but not from other types of auditory stimulus. However, for these synesthetes the color tends to depend on linguistic properties of the stimulus (e.g. the graphemic composition) rather than acoustic properties (e.g. Baron-Cohen et al., 1993; Paulesu et al., 1995). For example, heard words beginning with the letter 'P' may all tend to elicit the same color even when not starting by a /p/ sound (e.g. "psychology", "photo" and "potato" may have the same color). The present discussion will restrict itself to sound-vision synesthesia that depends on perceptual properties of the auditory stimulus, notably pitch.

One reason why this type of synesthesia has been regarded as of great interest is the suggestion that it may be present in all human infants. This raises the possibility that adult synesthetes have retained some pathways/processes that most other members of the population lost during development (e.g. Baron-Cohen, 1996; Maurer, 1997). In human infants, visual ERPs (event related potentials) to auditory stimuli decrease after six months but are still present at between 20 and 30 months of age (Neville, 1995). In kittens there is evidence of anatomical connections between primary auditory and visual areas that are lost as part of a pruning mechanism (Dehay et al., 1987, Innocenti et al., 1988). It may be genetically programmed given that it does not appear to depend on the presence of visual input (Innocenti et al., 1988). However, caution must be exerted in linking these findings to human synesthesia as inter-species differences are likely. More recent findings in the macaque suggest a lifelong presence of connections from primary auditory cortex to peripheral area V1, as well as from a polysensory temporal region to peripheral V1 (Falchier et al., 2002). It is also conceivable that the ERP effects in humans reflect developmental changes in the balance between feedback connections from multi-modal to unimodal regions rather than direct pathways between unimodal areas (Kennedy et al., 1997).

Our own research has addressed the question of shared processes between synesthetes and the normal population by looking at ways in which auditory properties (e.g. pitch, timbre) link with visual properties (e.g. the chromaticity and luminance of colors; Ward, Huckstep, & Tsakanikos, in press). Our reasoning was that if both synesthetes and controls perform the

task in similar ways then this would point to some shared processes between them. Such a finding would be more consistent with the view that synesthesia uses some of the same processes as normal cross-modal perception than the view that synesthetes have privileged mechanisms not present in others (except possibly in the earliest phase of development). Ward et al. (in press) presented 10 synesthetes and 10 controls with 70 tones of different pitch and timbre on several occasions. Given that controls do not report actual visual experiences, their task was to choose the ‘best’ hue to go with each tone. It was found that both groups showed an identical trend to associate low pitches with dark colors and high pitch with light colors (with luminance measured on the Munsell scale). This pattern was unaffected by differences in timbre. By contrast, differences in chroma (ranging from grayscale to high saturation colors) were associated with differences in timbre with pure tones judged to be less ‘colorful’ than musical tones. The highest values of chroma were found around middle C. Again, there were no differences between synesthetes and controls in the way that properties of the auditory stimulus were mapped on to visual properties.

Insert Figure 1 here

Our findings are consistent with previous research in the non-synesthesia literature showing a relationship between pitch and lightness (e.g. Marks, 1974; Marks, 1987; Hubbard, 1996), and with previous anecdotes from synesthetes (e.g. Marks, 1975). However, it represents the first direct comparison between these groups. Moreover, we were able to establish that in other key respects our synesthetes behaved differently. The synesthetes showed far greater internal consistency than controls (e.g. a control may choose light blue or light pink for the same tone on two occasions). Synesthetes, but not controls, appeared to generate colors automatically insofar as they showed Stroop-like interference for naming a colored patch incongruent with the color of a simultaneously presented tone (e.g. a blue color paired with a ‘red’ tone). In sum, our results point to some sharing of processes between synesthetes and the normal population but with some additional features required to explain the greater reliability and automaticity of the synesthetes.

There are a number of accounts of acquired sound-vision synesthesia. In some instances they are associated with visual field loss and the synesthetic experiences appear in the ‘blind’ region (Jacobs et al., 1981). These cases all had lesions to the peripheral visual system (optic nerve or chiasm). One patient exhibited this form of synesthesia with a medial temporal and midbrain tumor (Vike et al., 1984). There was no visual dysfunction and the synesthesia disappeared when the tumor was removed. These forms of acquired synesthesia possibly reflect an adjustment of the relative weightings between pre-existing unimodal auditory, unimodal visual and multi-modal regions but is less likely to reflect the development of entirely new pathways. Non-synesthetes who have been blindfolded for several days begin to experience visual hallucinations, some of which appear to be elicited by auditory stimuli (Merabet et al., 2004). In non-synesthetes, primary auditory areas can be activated by a unimodal visual stimulus (in silent lip reading; Calvert, 1997). Conversely, in non-synesthetes fitted with a cochlear implant due to deafness, activity in low-level visual areas (V1 and V2) is found when listening to unimodal auditory stimuli (Giraud et al., 2001). In both the studies of Calvert et al. (1997) and Giraud et al. (2001) the activity in primary auditory and visual areas was not reported to be associated with conscious auditory or visual experiences (although neither study explicitly discusses it). This may imply that the level of activity is below a threshold for conscious perceptual experience in these participants but raised above the threshold in the synesthetes. This remains speculative but plausible.

Vision-Touch Synesthesia

There is a wealth of evidence in the cognitive neuroscience literature pointing to a strong cross-modal interaction between vision and touch (for a review see Spence, 2002). For example, tactile acuity for stimuli applied to the arm is improved if the arm is visible, even though the mechanism producing the tactile stimulation cannot be seen (Kennett et al., 2001). Similarly, single cell recordings of monkeys have identified bimodal cells that respond to both touch and vision (Graziano et al., 1999).

Armel and Ramachandran (1999) documented an acquired case of synesthesia arising following retinal damage in which tactile stimulation of the arms induced color photisms. Interestingly, the intensity of the photisms was related to the location of the arms within the ‘visual’ field (remembering that the patient was blind) such that the synesthetic experiences were greater when the arms were in a normal field of view. This type of synesthesia has also been noted after cortical blindness (Goldenberg et al., 1995). The synesthetic images induced by tactile stimuli may have lead to a denial of blindness (anosognosia or Anton’s syndrome).

Conversely, synesthesia-like tactile and kinesthetic sensations have been induced in amputated limbs using mirrors (Ramachandran & Rogers-Ramachandran, 1996), in a limb with hemi-anesthesia whilst viewing real or video recorded tactile stimulations (Halligan et al., 1996), or in healthy limbs using adapting prisms (Mon-Williams et al., 1997). The fact that synesthesia-like sensations can be turned on or off (e.g. depending on the presence or absence of a mirror) implies that it reflects pre-existing mechanisms rather than reflecting longer term cortical changes.

We have recently documented a case of vision-touch synesthesia, C, that has a developmental rather than acquired origin (she reports having the sensations all her life and other family members possess synesthesia) (Blakemore et al., 2005). When C sees another person being touched she experiences tactile sensations on her own body. She does not report tactile sensations when inanimate objects are touched. This was investigated using fMRI. The study contrasted C’s brain activity to that of 12 controls when viewing a human face or neck being touched relative to viewing parts of inanimate objects (e.g. a fan) being touched. For controls, a ‘mirror touch’ circuit was activated when viewing humans touched relative to objects that included premotor regions, the primary and secondary somatosensory cortex, and the superior temporal sulcus (for related but not identical findings see Keysers et al., 2004). In C, the same circuit was activated but some regions (left premotor, primary somatosensory cortex) were activated to a much greater level than that observed in any of the individual control subjects. This implies that her synesthesia arises largely from the same system of mirror touch used by others but above a threshold for conscious tactile perception. There is, however, one caveat to this. Namely that C showed bilateral activation in the anterior insula that was not present in the control group. This may be linked to a self-attribution mechanism given that the region is activated when actions (e.g. Farrer & Frith, 2002) and memories (Fink et al., 1996) are attributed to oneself rather than another person.

Insert Figure 2 here

Synesthesia, Feature Binding, and Spatial Attention

Most synesthetes describe visual synesthetic experiences as seen in their mind’s eye. However, some synesthetes project these experiences externally (Dixon et al., 2004). In the case of chromatic-graphemic synesthesia – this usually means that the surface of visually presented graphemes appears colored. We therefore have a rather unusual instance of feature

binding: One in which color and shape are combined together although only the latter is actually presented to the perceiver.

The binding problem – how we combine together color, shape, and other surface features into objects – has been the center of much controversy (Wolfe & Cave, 1999). According to one influential view, binding of surface features is achieved by engaging spatial attention mechanisms (Treisman & Gelade, 1980). Indeed, under conditions of divided attention, binding may fail, giving rise to illusory conjunctions (e.g., Treisman & Schmidt, 1982) – correct registration of features of two or more objects, but incorrectly combining them (e.g., a lavender X and a chartreuse O might be perceived as a chartreuse X and a lavender O). Illusory conjunctions are more common when spatial attention is disrupted after brain damage (for review, see Robertson, 1999, 2003). One striking case, RM - a Balint's syndrome patient, exhibits illusory conjunctions even under free view conditions (e.g., Friedman-Hill, Robertson, & Treisman, 1995).

In a recent study we examined whether binding of externally projected synesthetic color to the evoking shape in chromatic-graphemic synesthesia obeys the rules of normal feature binding, i.e., whether spatial attention is necessary for binding of synesthetic color and the evoking grapheme (Sagiv, Heer, and Robertson, in press). One obvious reason to think that synesthetic color serves as another surface feature is that 'projecting' synesthetes describe it as such. Consistent with this, neuroimaging studies show that synesthetic color also activates the color area V4/V8 (Nunn et al., 2002; Sperling et al., in press).

First, we found that unlike ordinary (wavelength-derived) color, synesthetic color does not pop-out in visual search, i.e., synesthetic color is not available pre-attentively. Consistent with this, Laeng et al. (2004) showed that what seemed like pop-out of synesthetic color was actually restricted to trials in which the target was within the focus of attention. Edquist et al. (in press) also reached the conclusion that the evoking grapheme must be attended before synesthetic color arises.

Second, we showed that spatial attention modulates synesthesia: We presented irrelevant digit primes, followed by a colored target. While prime location was fixed throughout the experiment, target distance from fixation alternated between blocks (such that attention was either focused around fixation or distributed across a wider region). As expected, congruency of target color and the synesthetic color of the digit primes modulated color judgment times. Importantly, this effect was larger when attention was distributed across a wide area including the digit prime, than in the case in which spatial attention was allocated to a narrow region around fixation, leaving the synesthetic inducers outside the focus of attention.

We concluded that spatial attention does indeed play a key role in binding projected synesthetic color to the evoking grapheme and hypothesized that parietal mechanisms may be implicated. Indeed, in a follow-up transcranial magnetic stimulation (TMS) study, Esterman et al. (2004) reduced the interference of synesthetic color in a color naming task by stimulating the parieto-occipital junction. In sum, binding synesthetic colors to graphemes does involve attentional mechanisms necessary for ordinary feature binding.

The Time Course of Chromatic-Graphemic Synesthesia

Although synesthetic color may not be available preattentively, it does seem to arise as soon as the evoking stimulus is identified according to synesthetes' reports. Consistently with this, a wide range of studies suggest that the processes underlying synesthesia must be fairly rapid. At least, rapid enough to influence perception (Ramachandran & Hubbard, 2001a; Smilek et al., 2001; Palmeri et al., 2002; Blake et al., 2004), likely modulating activity in visual areas. While neuroimaging studies confirmed that synesthetic experience does

involve activation of visual cortex (Aleman et al, 2001; Nunn et al., 2002; Hubbard et al., 2005; Sperling et al, in press), little is known about the time course of processing in synesthesia.

Schiltz et al. (1999) recorded event-related potentials (ERPs) while synesthetes and non-synesthete control subjects viewed achromatic letters and numbers. They found that synesthetes had larger P300 components over frontal sites (for both target and non-target graphemes) compared with the control group. This relatively late time-course seems at odds with the dramatic effects synesthesia can have on perception of the evoking stimulus. Furthermore, Schiltz et al. fail to demonstrate involvement of posterior cortex. Because Schiltz et al. did not use a within-subject design, we cannot rule out the possibility that the group differences reflect some co-morbid neuropsychological factors rather than synesthesia per se.

Recently we ran another ERP study of synesthesia using a within-subject design (Sagiv et al., in preparation). We tested AD, a chromatic-graphemic synesthete (described further in Sagiv and Robertson, 2004). We recorded ERPs while she viewed centrally presented letters (one at a time). The letter stimuli, F and K, were either colored congruently with AD's synesthetic color (green and red, respectively) or incongruently with her synesthetic color (the color of the other letter). On 10% of the trials we presented a target letter (I, synesthetic color white). To ensure that AD's attention was focused on the presented letters, we requested her to report, at the end of each block, the number of Is presented.

Earlier EEG and MEG studies showed that responses to orthographic vs. non-orthographic material diverge at posterior temporal locations as early as 150-200msec after stimulus presentation (Bentin et al., 1999; Tarkiainen et al., 1999). We examined the N1/N170 component (150-170ms for AD) elicited by congruently and incongruently colored letters. Mean ERP amplitudes (relative to a nose reference) at this time range, in 8 blocks of trial were used as random factor. These were measured as PO7 and PO8, the posterior scalp locations at which the negative component N1 evoked by letters was maximal.

AD's N1 was significantly more negative in congruent than in the incongruent condition, showing for the first time an early effect of synesthesia on evoked potentials recorded over the posterior scalp, within an individual subject. Additionally, the N1 was larger on the right (PO8) than on the left (PO7) side, a somewhat unusual pattern for a right handed participant, however there was no interaction between congruency and hemisphere.

Insert Figure 3 here

What are origins of this congruency effect? Note that in both conditions a synesthetic color is induced. The only difference is whether we present letter-color combinations that match or mismatch AD's individual synesthetic correspondences. This could have implications on both perceived stimulus contrast and on stimulus categorization. The larger N1 recorded in the congruent condition is more consistent with the latter. Because AD reports seeing both her synesthetic color the actual stimulus color at the same time, the perceived contrast in the congruent condition (e.g., red on red) is lower than in the incongruent condition (e.g., red on green). On the other hand, the congruently colored letter may be easier to categorize. Thus, a more canonical stimulus form (at least for AD) may evoke larger N1. Alternatively, the effect may be due to attentional modulation.

While further studies will be required in order to understand the nature of this congruency effect, it is clear that it can serve as a marker for the time course of synesthesia. It may be useful as another tool for assessing individual differences among synesthetes

(Hubbard et al., 2005). Finally, the early modulation of posterior ERPs is consistent with the claim that synesthesia is a genuine perceptual phenomenon.

Number-Space Synesthesia

As many as 12% of the population experience numbers as occupying a particular spatial configuration (Seron et al., 1992). These have been termed number forms (Galton, 1880a,b). Although the overall direction of these forms is often left-to-right, the precise configuration can be idiosyncratic, as can their locations in space. For some, the number forms occupy peri-personal space around their body, for others it is in their ‘minds eye’. For some, the number forms are reported to move through space according to the number attended to, for others it is a static representation. We have recently provided some evidence for the authenticity of these subjective reports by showing that the task of deciding which of two numbers is larger is biased according to whether the two numbers are displayed in an arrangement that is congruent or incongruent with their number form (Sagiv et al., in press).

Insert Figure 4 here

Although number-space synesthesia does not involve one of the traditional five sensory modalities, it shares a number of similarities with other types of synesthesia. They are reported to be consistent over time, to come to mind automatically, and have no known origin. Our sense of space is clearly a perceptual dimension, although it is not tied to any one specific sense and may be represented at multiple levels in the brain (e.g. egocentric versus allocentric space) (e.g. Robertson, 2004). Sagiv et al. (in press) found that number-forms are far more prevalent in synesthetes who experience colors in response to numbers than in other members of the population or in other types of synesthesia. One account of this association is that the spatial attributes of numbers are applied to the associated synesthetic colors; thus, leading to a heightened awareness of a number-space relationship that, in most others, remains implicit. An alternative explanation is that number-space and number-color synesthesia are caused by the same underlying mechanisms (e.g. cross-activation of brain areas, in the case of numbers forms – in the parietal lobe). Indeed, similar regions in the parietal lobes are known to mediate both aspects of numerical cognition and spatial processing (Hubbard et al., 2005).

Evidence for a spatial (but typically implicit) mental number line in the normal population comes from the SNARC effect – the Spatial-Numerical Association of Response Codes (Dehaene et al., 1993). If participants are asked to make number judgments of parity (i.e. odd or even) about the numbers 1 to 9 then they are faster at making judgments about small numbers (<5) with their left hand and faster at making judgments about larger numbers (>5) with their right hand. Hence, participants perform as if reliant on a spatially-based mental number line running from left to right. In addition, it has been shown that passive viewing of numbers can induce spatial shifts of attention (Fischer et al., 2003) and that spatial attention deficits can bias numerical judgments (Vuilleumier et al., 2004). Consciously perceived number forms also tend to run from left to right, although they sometimes twist and turn (Sagiv et al., in press). The extent to which this is culturally biased is not entirely clear (the SNARC effect is reduced in Persian immigrants living in Paris; Dehaene et al., 1993). Number forms also occasionally point to cultural biases (e.g. 1 to 12 arranged like a clock). Nevertheless, it is conceivable that an association between numbers and space is universal even if direction in space is not.

Summary and Conclusions

The literature reviewed here points to a significant number of similarities between synesthetes and non-synesthetes in the way that different perceptual dimensions are linked together. This suggests that synesthesia is based on universal mechanisms rather than being based on mechanisms found solely in synesthetes. Although the review has been rather selective, there is evidence to suggest that the same holds in many other types of synesthesia including emotion-color correspondences (Ward, 2004), grapheme-color synesthesia (Rich et al., 2005; Simner et al., 2005), and the spatial representation of calendar time (Gevers et al., 2003; Sagiv et al., in press). Of course, synesthesia is different and any account of synesthesia must explain the differences between synesthetic and normal perception as well as the similarities. At least three differences are in need of explanation: phenomenology, automaticity and reliability. At present, it is unclear whether the fact that synesthetes have conscious perceptual experiences reflects quantitative increases in activity in critical brain regions or whether it reflects a more complex integration of several regions. Understanding these differences may provide some insights into the relationship between brain function and perceptual experience.

Cross-modal integration is obviously very useful for making inferences about objects and events in our environment. It seems, however, that this involves more than pathway convergence. In fact, there is a large body of evidence suggesting that activity in unimodal brain areas is modulated by information coming from other senses (e.g., Macaluso & Driver, 2005). One wonders whether the question should be why do so many people fail to experience synesthesia under normal conditions?

Still, lessons from synesthesia have even wider implications. Many aspects of cognition involve making some form of cross-domain correspondences. Language is one obvious example. Indeed, links between synesthesia, metaphor, creativity, and the origins of language have been suggested (e.g., Ramachandran & Hubbard, 2001b). Quite a few metaphors seem so intuitive that we may have forgotten that they link otherwise unrelated sensory modalities (e.g., “high pitch”, “future lies ahead”, “to be touched by your sentiments”, etc). Our ability to empathize is another example of cross-domain mapping. In this case an analogy is made between the self and others. Mirror-touch synesthesia may simply be an extreme form of this very basic capacity (yet still an interesting test case for theories of embodied cognition).

Number forms (as well as spatial descriptions of time) are found to be even more common than ‘standard’ synesthesia involving vision, touch, taste, smell, or sound. In this case, space is used not only as a ‘common currency’ for cross-modal interactions and binding different stimulus properties, but also as a dimension along which concepts can be mapped. How does space facilitate understanding of quantity? According to Walsh (2003), space, time, and quantity are all represented by a general magnitude processing system in the parietal lobe. We find, however, that synesthesia and spatial forms are commonly induced by ordinal sequences, including the letters of the alphabet – a category that is harder to describe in terms of magnitude. Instead we propose that use of space as an organizing principle, may be understood as a useful tool for grasping abstract concepts by constructing concrete spatial representations. Indeed, this too, could reflect a basic feature of human cognition, not only responsible for the SNARC effect (Dehaene et al., 1993) but also, the precursor of the use of graphic representation so prevalent in human culture.

Acknowledgements

The authors are supported by The Leverhulme Trust

References

- Aleman A., Rutten G.J., Sitskoorn M.M., Dautzenberg G., & Ramsey N.F. (2001). Activation of striate cortex in the absence of visual stimulation: an fMRI study of synesthesia. *Neuroreport*, 12: 2827-2830.
- Armel, K.C. & Ramachandran, V.S. (1999). Acquired synesthesia in retinitis pigmentosa. *Neurocase*, 5: 293-296.
- Baron-Cohen, S. (1996). Is there a normal phase of synaesthesia in development? *Psyche* 2. <http://psyche.cs.monash.edu.au/>
- Baron-Cohen, S., Burt, L., Smith-Laittan, F., Harrison, J., & Bolton, P. (1996). Synaesthesia: Prevalence and familiarity. *Perception*, 25: 1073-1079.
- Baron-Cohen, S., Harrison, J., Goldstein, L.H., & Wyke, M. (1993). Coloured speech perception: is synaesthesia what happens when modularity breaks down? *Perception* 22: 419-26.
- Bentin, S., Mouchetant-Rostaing, Y., Giard, M.H., Echallier, J.F., & Pernier, J. (1999). ERP manifestations of processing printed words at different psycholinguistic levels: time course and scalp distribution. *J. Cogn. Neurosci.*, 11: 235-60.
- Blake, R., Palmeri, T., Marois, R. & Kim, C.-Y. (2004). On the perceptual reality of synesthesia. In: L.C. Robertson & N. Sagiv (Eds.), *Synesthesia: Perspectives from Cognitive Neuroscience*. Oxford University Press, New York, pp 47-73.
- Blakemore, S.-J., Bristow, D., Bird, G., Frith, C., & Ward, J. (2005). Somatosensory activations during the observation of touch and a case of vision-touch synesthesia. *Brain*, 128: 1571-83.
- Calkins, M. W. (1895). Synaesthesia. *Am. J. Psychol.*, 7: 90-107.
- Calvert, G.A., Bullmore, E.T., Brammer, M.J., Campbell, R., Williams, S.C.R., McGuire, P.K., Woodruff, P.W.R., Iverson, S.D., & David, A.S. (1997). Activation of auditory cortex during silent lipreading. *Science*, 276: 593-96.
- Cohen-Kadosh, R., Sagiv, N., Linden, D.E.J., Robertson, L.C., Elinger, G., & Henik, A. (2005). When Blue is Larger than Red: Colors Influence Numerical Cognition in Synesthesia. *J. Cogn. Neurosci.*, 17: 1766-73.
- Cytowic, R. (1997). Synaesthesia: Phenomenology and neuropsychology? In S. Baron-Cohen & J.E. Harrison (Eds.) *Synaesthesia: Classic and contemporary readings*. Oxford: Blackwell, pp 17-39.
- Cytowic, R. E. (2002). *Synaesthesia: A Union of the Senses* (2nd Edition). MIT Press, Cambridge.
- Day, S. (2004). Some demographic and socio-cultural aspects of synesthesia. In: L.C. Robertson & N. Sagiv (Eds.), *Synesthesia: Perspectives from Cognitive Neuroscience*. Oxford University Press, New York, pp 11-33.
- Dehaene, S., Bossini, S., & Giraux, P. (1993). The mental representation of parity and numerical magnitude. *J. Exp. Psychol. Gen.*, 122: 371-396.
- Dehay, C., H. Kennedy, & Bullier, J. (1987). Characterization of transient cortical projections from auditory, somatosensory and motor cortices to visual areas 17, 18, and 19 in the kitten. *J. Comp. Neurol.*, 272: 68-89.
- Dixon, M.J. & Smilek, D. (2005). The importance of individual differences in grapheme-color synesthesia. *Neuron*, 45: 821-823.
- Dixon, M.J., Smilek, D., & Merikle, P.M. (2004). Not all synaesthetes are created equal: Projector vs. associator synaesthetes. *Cogn. Affect. Behav. Neurosci.*, 4: 335-343.
- Duffy, P.L. (2001). *Blue Cats and Chartreuse Kittens: How Synaesthetes Color their World*. Times Books, New York, pp.84-85.
- Edquist, J., Rich, A.N., Brinkman, C., & Mattingley, J.B. (in press). Do synaesthetic colors act as unique features in visual search? *Cortex*.
- Esterman, M., Verstynen, T., Ivry, R., and Robertson L.C. (2004) Attenuating the synesthetic experience with rTMS. Presented at the Fourth Annual American Synesthesia Association meeting, Berkeley, California, November 5-7.
- Falchier, A., Clavagnier, S., Barone, P., & Kennedy, H. (2002). Anatomical evidence of multimodal integration in primate striate cortex. *J. Neurosci.*, 22: 5749-5759.

- Farrer, C. & Frith, C.D. (2002). Experiencing oneself vs another person as being the cause of an action: The neural correlates of the experience of agency. *Neuroimage*, 15: 596-603.
- Fink, G.R., Markowitsch, H.J., Reinkemeier, M., Bruckbauer, T., Kessler, J., & Heiss, W.D. (1996). Cerebral representation of one's own past: Neural networks involved in autobiographical memory. *J. Neurosci.*, 16: 4275-4282.
- Fischer, M.H., Castel, A.D., Dodd, M.D., & Pratt, J. (2003). Perceiving numbers causes spatial shifts of attention. *Nat. Neurosci.*, 6: 555-556.
- Friedman-Hill, S.R., Robertson, L.C., & Treisman, A. (1995). Parietal contributions to visual feature binding: Evidence from a patient with bilateral lesions. *Science*, 269, 853-855.
- Galton, F. (1880a). Visualised numerals. *Nature*, 21: 252-256.
- Galton, F. (1880b). Visualised numerals. *Journal of the Anthropological Institute* 10: 85-102.
- Gevers, W., Reynvoet, B., & Fias, W. (2003). The mental representation of ordinal sequences is spatially organized. *Cognition*, 87: B87-B95.
- Ginsberg, L. (1923). A case of synaesthesia. *Am. J. Psychol.*, 34: 582-589.
- Giraud, A.L., Price, C.J., Graham, J.M., Truy, E., Frackowiak, R.S.J. (2001). Cross-modal plasticity underpins language recovery after cochlear implantation. *Neuron*, 30: 657-663.
- Goldenberg, G., Mullbacher, W., & Nowak, A. (1995). Imagery without perception: A case study of anosognosia for cortical blindness. *Neuropsychologia*, 33: 1373-1382.
- Graziano, M. S. A. (1999). Where is my arm? The relative role of vision and proprioception in the neuronal representation of limb position. *Proc. Natl. Acad. Sci. USA* 96: 10418-10421.
- Halligan, P.W., Hunt, M., Marshall, J.C., & Wade, D.T. (1996). When seeing is feeling: Acquired synaesthesia or phantom touch? *Neurocase*, 2: 21-29.
- Hartman, A.M., & Hollister, L.E. (1963). Effect of mescaline, lysergic acid diethylamide and psilocybin on color perception. *Psychopharmacologia*, 4, 441-451.
- Hubbard, E.M., A.C. Arman, Ramachandran, V.S., & Boynton, G.M. (2005). Individual differences among grapheme-color synaesthetes: Brain-behavior correlations. *Neuron*, 45: 975-985.
- Hubbard E.M., Piazza, M., Pinel, P., & Dehaene, S. (2005). Interactions between number and space in the parietal lobe. *Nat. Rev. Neurosci.*, 6: 435-448.
- Hubbard, T. L. (1996). Synesthesia-like mappings of lightness, pitch and melodic interval. *Am. J. Psychol.*, 109: 219-238.
- Innocenti, G. M., Berbel, P., Clarke, S. (1988). Development of projections from auditory to visual areas in the cat. *J. Comp. Neurol.*, 272: 242-259.
- Jacobs, L., Karpik, A., Bozian, D., & Gothgen, S. (1981). Auditory-visual synesthesia. Sound-induced photisms. *Arch. Neurol.*, 38: 211-216.
- Kennedy, H., Batardiere, A., Dehay, C., Barone, P. (1997). Synaesthesia: Implications for developmental neurobiology. In: S. Baron-Cohen & J.E. Harrison, *Synaesthesia: Classic and Contemporary Readings*, Blackwell, Oxford, pp 243-256.
- Kennett, S., Taylor-Clarke, M., Haggard, P. (2001). Noninformative vision improves the spatial resolution of touch in humans. *Curr. Biol.*, 11: 1188-1191.
- Keysers, C., Wicker, B., Gazzola, V., Anton, J.L., Fogassi, L., & Gallese, V. (2004). A touching sight: SII/PV activation during the observation and experience of touch. *Neuron*, 42: 335-346.
- King, A.J. & Calvert, G.A. (2001). Multisensory integration: Perceptual grouping by eye and ear. *Curr. Biol.*, 11: R322-R325.
- Knoch, D., Gianotti, L.R., Mohr, C., & Brugger, P. (2005). Synesthesia: When colors count. *Cogn Brain Res.* 25: 372-4.
- Laeng, B., Svartdal, F., & Oelmann, H. (2004). Does color synesthesia pose a paradox for early-selection theories of attention? *Psychol. Sci.*, 15: 277-81.
- Macaluso, E. & Driver, J. (2005) Multisensory spatial interactions: a window onto functional integration in the human brain. *Trends Neurosci.*, 28: 264-271.
- Marks, L.E. (1974). On associations of light and sound: The mediation of brightness, pitch, and loudness. *Am. J. Psychol.*, 87: 173-188.
- Marks, L. E. (1975). On coloured-hearing synaesthesia: Cross-modal translations of sensory dimensions. *Psychol. Bull.*, 82: 303-331.
- Marks, L.E. (1987). On cross-modal similarity: Auditory-visual interactions in speeded discrimination. *J. Exp. Psychol. Hum. Percept. Perform.*, 13: 384-394.

- Martino, G., & Marks, L.E. (2001). Synesthesia: Strong and weak. *Curr. Dir. Psychol. Sci.*, 10: 61-65.
- Maurer, D. (1997). Neonatal synaesthesia: Implications for the processing of speech and faces. In: S. Baron-Cohen & J.E. Harrison, *Synaesthesia: Classic and Contemporary Readings*, Blackwell, Oxford, pp 224-242.
- Merabet, L.B., Maguire, D., Warde, A., Alterescu, K., Stickgold, R., Pascual-Leone, A. (2004). Visual hallucinations during prolonged blindfolding in sighted subjects. *J. Neuroophthalmol.*, 24: 109-113.
- Mills, C.B., Howell Boteler, E., & Oliver, G.K. (1999). Digit synaesthesia: A case study using a stroop-type test. *Cogn. Neuropsychol.*, 16: 181-191.
- Mon-Williams, M., Wann, J.P., Jenkinson, M., & Rushton, K. (1997). Synaesthesia in the normal limb. *Proc. Biol. Sci.*, 264: 1007-1010.
- Myles, K.M., Dixon, M.J., Smilek, D., & Merikle, P.M. (2003). Seeing double: The role of meaning in alphanumeric-color synaesthesia. *Brain Cogn.*, 53: 342-345.
- Neville, H.J. (1995). Developmental specificity in neurocognitive development in humans. In: M. Gazzaniga, *The Cognitive Neurosciences*. MIT Press, Cambridge.
- Nunn, J.A., Gregory, L.J., Brammer, M., Williams, S.C.R., Parslow, D.M., Morgan, M.J., Morris, R.G., Bullmore, E.T., Baron-Cohen, S., & Gray, J.A. (2002). Functional magnetic resonance imaging of synesthesia: activation of V4/V8 by spoken words. *Nat. Neurosci.*, 5: 371-5.
- Palmeri, T.J., Blake, R., Marois, R., Flanery, M.A., & Whetsell, W. Jr. (2002). The perceptual reality of synesthetic colors. *Proc. Natl. Acad. Sci. USA*, 99: 4127-31.
- Paulesu, E., Harrison, J., Baron-Cohen, S., Watson, J.D. G., Goldstein, L., Heather, J., Frackowiak, R.S.J. & Frith, C.D. (1995). The physiology of coloured hearing: A PET activation study of color-word synaesthesia. *Brain*, 118: 661-676.
- Ramachandran, V.S. & Hubbard, E.M. (2001a). Psychophysical investigations into the neural basis of synaesthesia. *Proc. Biol. Sci.*, 268: 979-983.
- Ramachandran, V.S. & Hubbard, E.M. (2001b). *Synaesthesia - A Window Into Perception, Thought and Language*. *J. Conscious. Stud.*, 8: 3-34.
- Ramachandran, V.S. and Rogers-Ramachandran, D. (1996). Synaesthesia in phantom limbs induced with mirrors. *Proc. Biol. Sci.*, 263: 377-386.
- Rich A.N., Bradshaw J.L., & Mattingley J.B. (2005) A systematic, large-scale study of synaesthesia: implications for the role of early experience in lexical-color associations. *Cognition*.
- Robertson, L.C. (2003). Binding, spatial attention and perceptual awareness. *Nat. Rev. Neurosci.*, 4: 93-102.
- Robertson, L.C. (2004). *Space, Objects, Minds and Brains*. Psychology Press, Hove.
- Robertson, L.C. (1999). What can spatial deficits teach us about feature binding and spatial maps? *Vis. Cogn.*, 6: 409-430.
- Sagiv, N., & Ben-Tal, O. (in preparation). Nocturnal synesthesia.
- Sagiv, N. (2004). Synesthesia in perspective. In: L.C. Robertson & N. Sagiv (Eds.), *Synesthesia: Perspectives from Cognitive Neuroscience*. Oxford University Press, New York, pp.3-10.
- Sagiv, N., Heer, J., Robertson, L.C. (2006). Does binding of synesthetic color to the evoking grapheme require attention? *Cortex* 42: 232-242.
- Sagiv, N. & Robertson, L.C. (2004). Synesthesia and the Binding Problem. In: L.C. Robertson & N. Sagiv (Eds.), *Synesthesia: Perspectives from Cognitive Neuroscience*. Oxford University Press, New York, pp.90-107.
- Sagiv, N., Simner, J., Collins, J., Butterworth, B., & Ward, J. (2006). What is the relationship between synaesthesia and visuo-spatial Number Forms? *Cognition* 101: 114-128.
- Schiltz, K., Trocha, K., Wieringa, B.M., Emrich, H.M., Johannes, S. & Munte, T.F. (1999). Neurophysiological aspects of synesthetic experience. *J Neuropsychiatry Clin Neurosci*, 11: 58-65.
- Seron, X., Pesenti, M., Noel, M.-P., Deloche, G., & Cornet, J.A. (1992). Images of numbers, or "when 98 is upper left and 6 sky blue". *Cognition*, 44: 159-196.
- Shanon, B. (1982). Color associates to semantic linear orders. *Psychol. Res.* 44: 75-83.
- Shanon, B. (2002). *The Antipodes of the Mind: Charting the Phenomenology of the Ayahuasca Experience*. Oxford University Press, Oxford, pp 189-190, 337-338.
- Shanon, B. (2003). Three stories concerning synesthesia. A reply to Ramachandran and Hubbard. *J. Conscious. Stud.*, 10:69-74.

- Simner, J., Ward, J., Lanz, M., Jansari, A., Noonan, K., Glover, L., & Oakley, D.A. (2005). Non-random associations of graphemes to colours in synaesthetic and non-synaesthetic populations. *Cogn. Neuropsychol.* 22: 1069-85
- Simner, J., Mulvenna, C., Sagiv, N., Tsakanikos, E., Witherby, S.A., Fraser, C., Scott, K., & Ward J. (2006). Synaesthesia: The prevalence of atypical cross-modal experiences. *Perception* 35: 1024-1033.
- Smilek, D., Dixon, M.J., Cudahy, C., & Merikle, P.M. (2001). Synaesthetic photisms influence visual perception. *Journal of Cognitive Neuroscience*, 13: 930-936.
- Spence, C. (2002). Multisensory attention and tactile information-processing. *Behav. Brain Res.*, 135: 57-64.
- Sperling, J.M., Prvulovic, D., Linden, D.E.J., Singer, W., & Stirn, A. (in press). Neuronal correlates of graphemic color synaesthesia: A fMRI study. *Cortex*.
- Steven M.S. and Blakemore C. (2004). Visual synesthesia in the blind. *Perception*, 33: 855-868.
- Tarkiainen, A., Helenius, P., Hansen, P.C., Cornelissen, P.L., & Salmelin, R. (1999). Dynamics of letter string perception in the human occipitotemporal cortex. *Brain*, 122: 2119-2132.
- Treisman, A. & Gelade, G. (1980). A feature integration theory of attention. *Cogn. Psychol.*, 12: 97-136.
- Treisman, A. & Schmidt, H. (1982). Illusory conjunctions in the perception of objects. *Cogn. Psychol.*, 14: 107-141.
- Uhlich, E. (1957). Synesthesia in the two sexes. *Z. Exp. Angew. Psychol.* 4: 31-57.
- Vike, J., Jabbari, B., Maitland, C.G. (1984). Auditory-visual synesthesia: Report of a case with intact visual pathways. *Arch. Neurol.*, 41: 680-681.
- Vuilleumier, P., Ortigue, S., & Brugger, P. (2004). The number space and neglect. *Cortex*, 40: 399-410.
- Walsh, R. (2005). Can synesthesia be cultivated? Indications from surveys of meditators. *J. Conscious. Stud.*, 12: 5-17.
- Walsh, V. (2003). A theory of magnitude: common cortical metrics of time, space and quantity. *Trends Cogn. Sci.*, 7: 483-488.
- Ward, J. (2004). Emotionally mediated synaesthesia. *Cogn. Neuropsychol.*, 21: 761-772.
- Ward, J., Huckstep, B., Tsakanikos, E. (in press). Sound-color synaesthesia: To what extent does it use cross-modal mechanisms common to us all? *Cortex*.
- Ward, J. & Simner, J. (2005). Is synaesthesia an X-linked dominant trait with lethality in males? *Perception* 34: 611-623.
- Wolfe, J.M. & Cave, K.R., (1999). The psychophysical evidence for a binding problem in human vision. *Neuron*, 24: 11-17.

Cite as:

Sagiv, N & Ward, J. (2006). Cross-modal interactions: lessons from synesthesia. In Martinez-Conde, S., Macknik, S.L., Martinez, L.M., Alonso, J-M., & Tse, P.U. (Eds). *Progress in Brain Research*, Vol. 155 (263-275). London: Elsevier Science.

Formatted PDF available from Elsevier at:

[http://dx.doi.org/10.1016/S0079-6123\(06\)55015-0](http://dx.doi.org/10.1016/S0079-6123(06)55015-0)

Figure legends

Figure 1: Both sound-color synesthetes and non-synesthetic controls show the same trend (no group difference: $F(1,18)=2.51$, N.S.) to associate low pitch tones with darker colors (low Munsell values) and high pitch tones with lighter colors (higher Munsell values). Figure reprinted from Ward et al. (in press), Sound-color synaesthesia: To what extent does it use cross-modal mechanisms common to us all? *Cortex*, by permission of Masson.

Figure 2: Activation of the SI head area ($x=60$, $y=-15$, $z=48$) in non-synesthetic controls arising from observing touch to a human face (relative to a human neck). The same region was over-activated in synesthete C, and was also active when participants were physically touched on the face. Figure reprinted from Blakemore et al., Somatosensory activations during the observation of touch and a case of vision-touch synesthesia, *Brain*, 1995, 128(7), 1571-83, by permission of Oxford University Press.

Figure 3: Event-related potentials evoked by letter stimuli colored either congruently or incongruently with AD's synesthetic colors. The approximate location of scalp locations (PO7 and PO8) is shown on the schematic drawing on the lower left.

Figure 4: An example of a more convoluted number form drawn by one of our synesthetes (colors not shown).

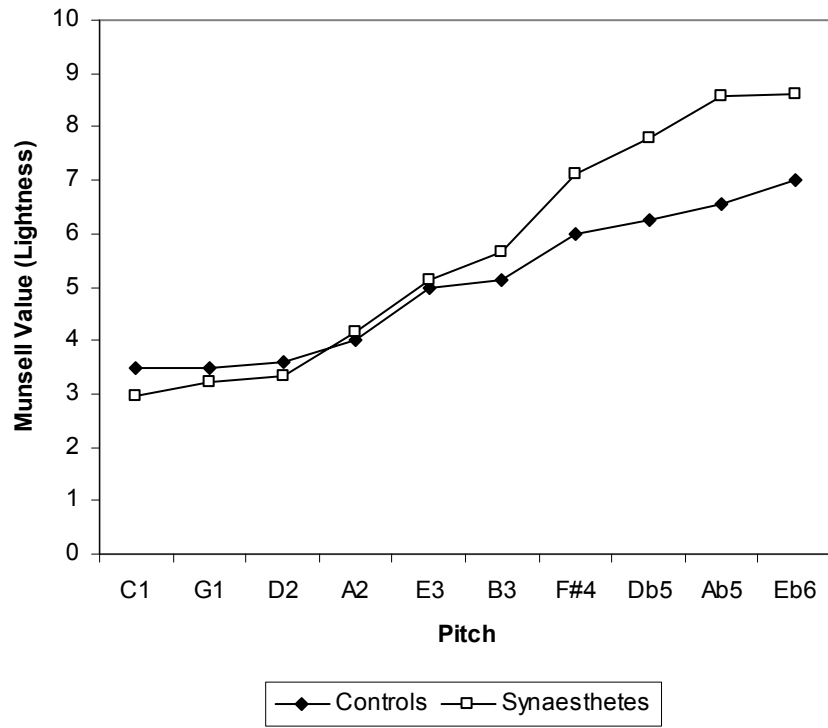


Figure 1

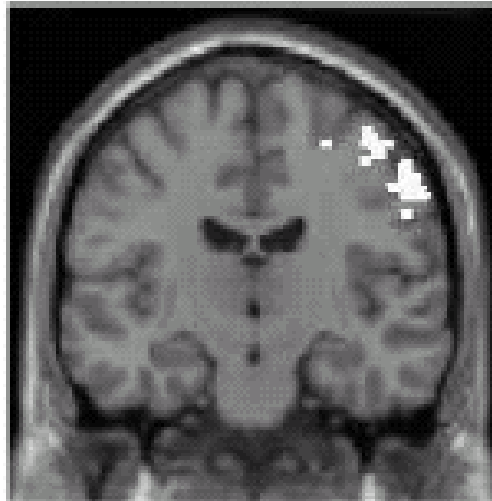


Figure 2

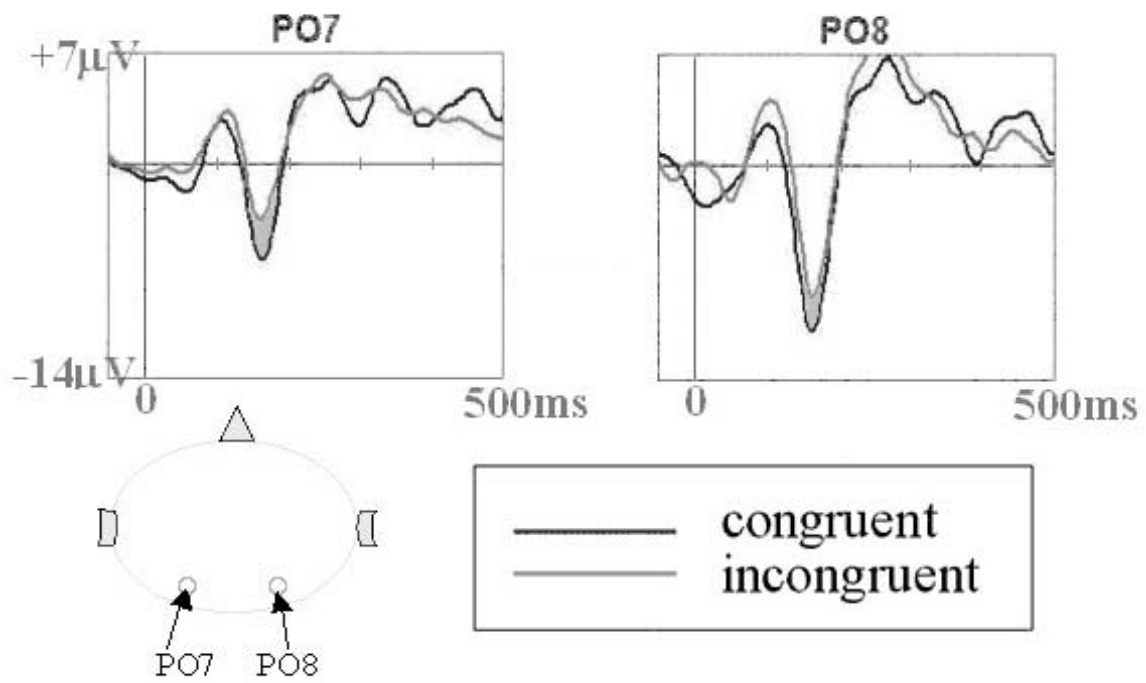


Figure 3

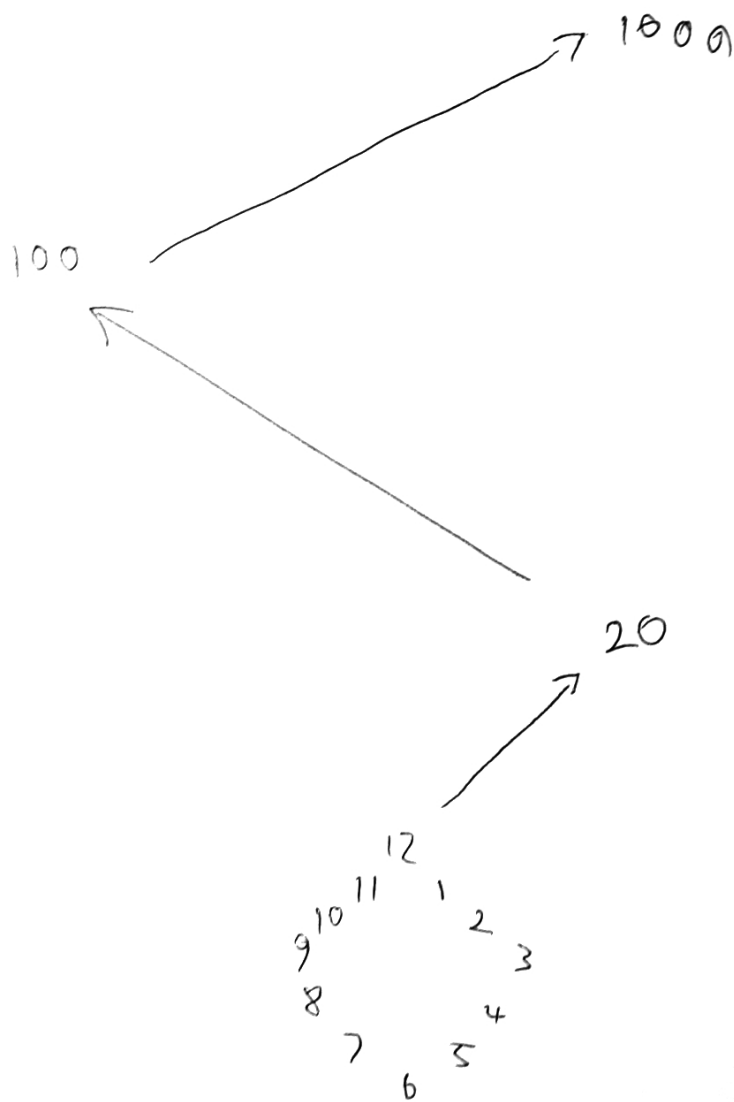


Figure 4