McLeod P, Plunkett K and Rolls E (1998) *Introduction to Connectionist Modelling of Cognitive Processes*. Oxford: Oxford University Press.
Minsky M (1968) *Semantic Information Processing*. Cambridge, MA: MIT Press.
Rolls ET and Treves A (1998) *Neural Networks and Brain Function*. Oxford: Oxford University Press.
Rosenbloom PS, Laird JE and Newell A (eds) (1993) *The Soar Papers: Research on Integrated Intelligence*. Cambridge, MA: MIT Press.
Wagman M (1997) *The General Unified Theory of Intelligence: Its Central Conceptions and Specific Application to Domains of Cognitive Science*. Westport, CT: Praeger.

Synaesthesia

Intermediate article

Simon Baron-Cohen, University of Cambridge, Cambridge, UK
John Harrison, Cambridge Psychometric Consultants, Cambridge, UK

CONTENTS

Synaesthesia is experienced when stimulation of one sensory modality gives rise to a perception in a second modality, without that second modality having received any direct stimulation.

WHAT IS SYNAESTHESIA?

Synaesthesia occurs when stimulation of one sensory modality automatically triggers a perception in a second modality, in the absence of any direct stimulation to this second modality (Vernon, 1930; Marks, 1975; Cytowic, 1989, 1993; Motluk, 1994). So, for example, a sound might automatically and instantly trigger the perception of vivid color, or vice versa. The woman EP, the subject of Baron-Cohen *et al.*'s (1987) study, provided a number of descriptions of color–word correspondences, describing the sound of the word MOSCOW as 'Darkish grey, with spinach green and pale blue'. Those with the condition describe the percept not as part of their external visual experience, nor in their 'mind's eye', but somewhere else, phenomenologically.

Many combinations of synaesthesia are reported to occur naturally, including sound giving rise to visual percepts ('colored-hearing') and smell giving rise to tactile sensation, as in Cytowic's (1993) subject MW. Colored-hearing synaesthesia appears to be the most common form. Certain combinations of synaesthesia almost never occur (e.g. touch to hearing). Synaesthesia is also sometimes reported by those who have used hallucinogenic drugs, such as Lysergic Acid Diethylamide (LSD) or mescaline. This article will focus on the naturally occurring form of synaesthesia, whilst acknowledging that there may be a connection to be found with the drug-induced form.

Terminology

'Developmental' synaesthesia

'Developmental synaesthesia' is distinct from acquired synaesthesia (of which there are at least two forms) and pseudosynaesthesia. Developmental synaesthesia in most cases has several characteristics: (1) it has a childhood onset, in all cases before four years of age; (2) it is different from hallucination, delusion, or other psychotic phenomena; (3) it is different from imagery arising from imagination; (4) it is not induced by drug use; it is (5) vivid; (6) automatic/involuntary; and (7) unlearnt.

Synaesthesia caused by neurological dysfunction

A variety of neuropathological conditions can give rise to acquired synaesthesia. A full account of the varieties of acquired synaesthesia is given in Critchley (1994). Note that the resultant synaesthesic percepts are often much simpler than the complex forms seen in developmental synaesthesia.

Synaesthesia as a consequence of psychoactive drug use

Synaesthesia can result from the use of psychoactive drugs (Cytowic, 1989). The mechanisms by which drug-induced synaesthesia occur are not well understood, though the use of LSD, mescaline, and psilocin are all reported to cause confusion between the sensory modalities, so that sounds are perceived as visual (Rang and Dale, 1987). Neurophysiological studies reported by Aghajanian (1981) suggest different sites of action for LSD and mescaline, with LSD seeming to work by inhibiting the serotonin-containing neurons of the raphe nuclei, and mescaline by acting upon the noradrenergic system. Drug-induced synaesthesia differs from developmental synaesthesia in several ways: (1) it is often accompanied by hallucinations and loss of reality-monitoring; (2) it is transient; (3) it usually has an onset only in adult life (or whenever the drug was used); and (4) it can produce sensory combinations which do not otherwise occur naturally.

What Synaesthesia Is Not

Metaphor

Almost all writers on the topic of synaesthesia have been drawn into discussion of the possibility that a number of authors, poets, artists, and musicians may have had synaesthesia. A typical list of these individuals would include the composers Liszt, Rimsky-Korsakov, Messiäen, and Scriabin; the poets Basho, Rimbaud, and Baudelaire; the artists Kandinsky and Hockney; and, finally, the novelist Nabokov. There is no evidence of these individuals having been tested formally for synaesthesia. Much of the literature may instead reflect a form of metaphor or analogy. Thus, Charles Baudelaire appears to have believed in the unity of sensation (as implied by his poem 'Correspondances'). Metaphor is widespread in language and provides ripe conditions for confusion with developmental synaesthesia. Distinguishing the 'metaphor as pseudosynaesthesia' from developmental synaesthesia relies on objective tests. However, the key differences are that in metaphor: (1) no percept is *necessarily* triggered; (2) the subject will often acknowledge that the description is only an analogy; and (3) it is voluntary.

Association

A second form of pseudosynaesthesia includes individuals who have simply learnt to pair words/letters with colors (e.g. alphabet books in which letters are depicted in a variety of colors). Detailed examination of the color-letter alphabets of individuals with developmental synaesthesia often yields the finding that successive letters have very similar colors. This is in marked to contrast to colored alphabet books in which successive letters have markedly different color representations.

HISTORY

The closing decades of the nineteenth century saw a considerable number of accounts of synaesthesia, most notable amongst which was Galton's (1883) *Inquiries into Human Faculty and Its Development*. Scientific interest in the condition declined with the rise of behaviorism and very little on the topic appears in the literature from the late 1920s onward. This was probably because behaviorism banished reference to mental states from scientific language. As synaesthesia could only be defined by self-report and reference to mental states, it was not considered 'scientific'.

Since the 1990s synaesthesia research has enjoyed something of a renaissance. Various disciplines within cognitive neuroscience have contributed both new data and theory. Such developments have led to the condition being widely recognized as having a neurological reality. This new acceptance of the condition is in part due to objective approaches to studying it now being available.

EXPERIMENTAL WORK ON SYNAESTHESIA IN PSYCHOLOGY AND NEUROSCIENCE

The conventional test for the colored-hearing synaesthesia involves assessing a subject's *consistency* in reporting color descriptions for words across two or more occasions, when the subject has no prior warning of the retest. This consistency should be irrespective of the length of interval between testing sessions (Baron-Cohen *et al*, 1987; Baron-Cohen *et al*., 1993). Using this method, consistency is typically as high as 90 per cent, even when retested over years and even when stringent criteria are set for retest descriptions.

The advent of neuroimaging techniques such as positron emission tomography (PET) and functional magnetic resonance imaging (fMRI) has also provided an opportunity to image the brains of individuals with synaesthesia *in vivo*. Cytowic used the xenon inhalation technique to image the brain of a single subject (Cytowic and Wood, 1982) and others have used PET (Paulesu *et al*., 1995) and

more recently fMRI (Gray *et al*., 1997). Given the marked consistency of patterns of activation in synaesthetes studied in the Paulesu *et al*. study, it might ultimately prove possible to determine the presence of synaesthesia objectively using functional brain imaging techniques. The neuroimaging data is discussed later in relation to theories of synaesthesia.

THEORIES OF SYNAESTHESIA

Over the past 200 years a number of hypotheses have been put forward to explain the cause of synaesthesia.

Preserved Neural Connectivity

The normal adult human brain does not contain direct neural connections between auditory and visual areas. However, the early developing brain in many species does. This first theory holds that, probably for genetic reasons, in individuals with synaesthesia, pathways between auditory and visual areas in the brain continue to exist beyond neoteny, such that when words, or sounds, give rise to activation in auditory areas, visual cortex is also stimulated.

There is evidence for the presence of such connective pathways in other species (see Kennedy *et al*., 1996). Kennedy and others in a number of studies (Dehay *et al*., 1984; Kennedy *et al*., 1989), have found that connections between auditory and visual areas exist in the brain structure of species such as the macaque monkey (*Macaca irus*) and the domestic cat (*Felis domesticus*). These projections appear to be transient, typically disappearing approximately three months *post partum*.

There is also some evidence that these transitory pathways exist in human neonates, and may, as in cats and macaques, get 'pruned' as part of the biological maturation of the brain. Much of this evidence is reviewed by Maurer (1993). Maurer's hypothesis is that human babies mix the input from different senses and that this gives rise to normal 'synaesthesia'. We know from the work by Meltzoff and Borton (1979) that babies who suck on either a 'nubby' or a 'smooth' pacifier (dummy) will prefer to look at a picture of the pacifier they sucked on, thereby showing a match between touch and vision. The Meltzoff and Borton study is usually taken as evidence for cross-modal transfer. Maurer goes one step further in suggesting that synaesthesia might be a normal stage of perceptual experience in addition to cross-modal transfer.

Maurer's evidence in support of this view comes from other studies of neonates. One such study is that reported by Lewkowicz and Turkewicz (1980). In this experiment one-month-old children, who had seen a patch of white light for 20 trials, were presented with bursts of 'white noise' presented at different intensities. During the noise presentation, the patch of light that they had been trained on was interspersed repeatedly and the children's heart rate was measured. Normally heart rate increases as a function of noise intensity, but Lewkowicz and Turkewicz found that the heart rate recorded at a noise intensity of 74 dB showed the lowest heart rate change and that for values greater or less than this value heart rate increased. Lewkowicz and Turkewicz's interpretation of this finding was that 'infants were responding to the auditory stimuli in terms of their similarity to the previously presented visual stimulus' (1980, p. 597), or, as Maurer put it, 'the children responded least to the "familiar" intensity' (p. 110). Maurer also cites evidence from electrophysiological studies of neonates showing that the amplitude of somatosensory evoked potentials increases when they are played white noise. Normally, these potentials only increase as a consequence of tactile stimulation. Finally, she cites the work of Neville (1993) that in early infancy auditorily evoked potentials to language evoke a potential in the occipital cortex, whereas in older individuals these stimuli yield potentials only in auditory areas such as the temporal lobes.

The evidence in this section is consistent with the notion that synaesthesia might be due to the persistence of neural information passing from auditory to visual brain areas, beyond the neonatal stage. Taken in the context of development, it also suggests the intriguing possibility that we might *all* be colored-hearing synaesthetes until we lose connections between these two areas somewhere about three months of age, at which point cortical maturation gives rise to sensory differentiation. This is consistent with Cytowic's (1989) view of synaesthetes being 'cognitive fossils'.

Sensory Leakage Theory

Jacobs *et al*. (1981) proposed what can be called the 'Sensory Leakage Theory'. This is an account of how simple photisms arise in cases of acquired synaesthesia, though it could in principle be extended to account for developmental synaesthesia. As mentioned earlier, most cases of *acquired* synaesthesia arise in individuals who suffer brain damage to anterior portions of the brain, often the optic nerve. Close examination of the nine patients

reported in Jacobs *et al*. reveals that four of these patients (cases 1, 2, 4, 7) also experienced photisms in the *absence* of auditory stimulation, casting doubt on whether these instances should be described as cases of auditory-visual synaesthesia at all. It is also worth observing that seven patients always experienced their photisms when they were 'relaxed, drowsy or dozing' (p. 214), circumstances in which hypnagogic hallucinations are possible.

The essence of Jacobs *et al*.'s theory is that auditory information 'leaks' into pathways and areas in the brain that ordinarily deal with visual information. Jacobs *et al*. expand this 'leakage' theory by suggesting that there are 'numerous regions of the brain where visual and auditory pathways lie in close anatomic proximity' (p. 216) and that at these points post-synaptic fibres might converge to cause the synaesthesia seen in a range of pathological states such as congenital blindness and drug intoxication.

Evidence to support leakage between areas subserving different forms of sensory information is sparse, causing some difficulties for Jacobs *et al*.'s theory. However, recent work has suggested that rather than posit the need for leakage, it is possible to find at certain locations in the brain classes of neurons that are responsive to stimulation from more than one sensory modality. For example, in a study of nonhuman primates carried out by Graziano *et al*. (1994), recordings were made from neurons (N = 141) in the ventral portion of the premotor cortex. Of these neurons, 27 to 31 per cent were found to be bimodally responsive, firing as a result of either, or both, visual and somasthetic stimulation.

Sadato *et al*. (1996) showed that congenitally blind subjects show increased bloodflow to primary visual areas when reading Braille, a finding the authors account for by suggesting that in these subjects 'cortical areas normally reserved for vision may be activated by other sensory modalities' (p. 526). Such an account might also explain the case of acquired synaesthesia reported by Rizzo and Eslinger (1989). Their subject, a 17-year-old who had developed retrolental fibroplasia as the consequence of perinatal difficulties, exhibited a florid form of colored hearing for musical tones. Rizzo and Eslinger failed to find evidence to suggest visual area activation as a consequence of auditory stimulation, but limited themselves to the use of electroencephalography as a means of detecting such activity. The Sadato *et al*. finding suggests that functional neuroimaging might prove to be a useful technique for investigating cases of acquired synaesthesia.

Cytowic's Theory of Synaesthesia

The most controversial theoretical account of the cause of synaesthesia is that most recently advanced by Cytowic (1993) in his book *The Man Who Tasted Shapes*. Cytowic proposes that synaesthesia occurs because 'parts of the brain get disconnected from one another … causing the normal processes of the limbic system to be released, bared to consciousness, and experienced as synaesthesia' (p. 163). His assertion that the limbic system is the critical brain locus can and has been tested. In the final chapter, Cytowic concedes that whilst he has no direct evidence to implicate a particular neural structure, given the 'stunning shut-down of the cortex' (p. 152) observed in the ^{133}Xenon studies of blood flow in the subject MW's brain, he points to the limbic areas as being 'the seat of synaesthesia'. Direct evidence of the involvement of the limbic system would have been provided by evidence of blood flow changes in this brain region, though unfortunately neuroimaging using ^{133}Xenon inhalation does not permit such deep structures to be imaged.

This is not a limitation shared by PET and so the importance of the limbic system in synaesthesia can be evaluated using this technique. This was one of the questions addressed in the study of colored-hearing synaesthesia reported by Paulesu *et al*. (1995). This study compared brain activity in synaesthetes and control subjects whilst listening to either words or pure tones. The synaesthetes reported color percepts for words but not for nonword sounds, and so a comparison of brain activation on synaesthetes listening to words as compared with tones, and with control subjects, should yield clues to the neural basis of colored-hearing synaesthesia. From this analysis two areas of particular interest emerged, posterior infertemporal cortex and the parietal-occipital junction, both of which have known involvement in color perception. However, in neither the between-groups nor the within-groups comparisons was there any suggestion of limbic system involvement. Of course it might be that Cytowic's subject MW is different in *kind* from the subjects scanned by Paulesu *et al*. Given MW's grossly abnormal resting blood flow levels, together with his polymodal synaesthesia, this remains a strong possibility.

The Learned Association Theory

This theoretical proposition was originally suggested as an explanation of synaesthesia by Calkins (1893) and holds that in colored-hearing

synaesthesia, the color–word and/or sound correspondences reported are due entirely to learned association. The idea is that the color–letter associations are derived from colored alphabet books, or colored letters, that the individual saw as a child. Whilst this is a plausible account of the acquisition of pseudosynaesthesia, we suspect, for a number of reasons, that it is an unsatisfactory account of developmental synaesthesia. Reasons include the following:

1. The sex ratio. The sex ratio in synaesthesia is 6:1 (f:m). Why should so many more women, as compared to men, form such associations? A socialization account which would lead to this sex ratio is not immediately obvious, though transmission from mothers to daughters via modeling may be a possibility (though a tenuous one).
2. Consecutive letters. Careful scrutiny of the 'colored alphabets' of many synaesthetes, yields the finding that often consecutive letters are closely described in color terms (e.g. 'M' = olive green, 'N' = emerald green, 'O' = washed-out pale green). When compared to colored alphabet books, it is found that publishers logically go to great lengths to ensure that consecutive letters are printed in very different colors. Learned association therefore cannot account for the specific colors of particular letters or phonemes.
3. Synaesthesic twins. A comparison of the colored alphabets of twins so far has yielded substantial variation in the color–letter correspondences made by each of the pair. The same variation is also seen among siblings and by mothers and daughters in the same family. It is surprising that there is not greater similarity in the color–letter correspondences of family members if colored alphabets are acquired as learned associations.
4. Lack of recollection. Most people with synaesthesia are unable to report *knowing* that their letter–color associations were learnt either purposefully or incidentally via exposure to colored alphabet letters or books.

The learned association theory of synaesthesia has not yet provided satisfactory explanations of these anomalies.

The Genetic Theory of Synaesthesia

The possibility that synaesthesia might be an inherited trait seems to have first been put forward by Galton (1883). Genetic mechanisms might cause the preserved neural connectivity described above. Earlier we reviewed the evidence for transitory connections between auditory and visual brain areas in other mammalian species. Assuming that such connections are also to be found in our species, one explanation for synaesthesia is that in individuals with the condition these neonatal pathways persist due to inherited mechanisms. A recent study (Baron-Cohen *et al*., 1996) has provided evidence to support the notion that synaesthesia might be an inherited trait. In that study, the pedigrees of seven families of probands suggested that the condition is inherited.

If the genetic theory is supported, this begs the question of by what mechanism such a biological inheritance has its effect. A candidate mechanism would be the expression of genes that regulate the migration and maturation of neurons within the developing brain. A second candidate mechanism is 'neuronal pruning' (apoptosis). On this account synaesthesia can be best explained not by positive forces creating neural pathways that in non-synaesthetes do not exist, but by maturational effects that lead to neonatal pathways being left active. This would be consistent with Maurer's observations regarding the emergence of modality-specific responses in three-month-old human neonates.

The Cross-modal Matching Theory

This is based on evidence of cross-modal matching in normal subjects, in addition to those found by Lewkowicz and Turkewicz described earlier. Much of the work looking at cross-modal analogs of characteristics such as brightness/loudness, etc. has been carried out by Marks (Marks, 1982a, b, 1987).

Marks (1982a) showed that normal subjects exhibited remarkable consistency when asked to rate a selection of auditory-visual synaesthetic metaphors using scaled ratings of loudness, pitch, and brightness. For example, 'sunlight' was rated as louder than 'glow', which was in turn rated as louder than 'moonlight'. A second study reported by Marks (1982b) required subjects to set the loudness of a 1000-Hz tone and the brightness of white light for 15 cases of visual-auditory metaphor taken from works of poetry. Again, marked consistency characterized the performance of these subjects, leading Marks to propose that intensity might be a common sensory dimension.

The Modularity Theory

In order for us to 'know' that a percept is visual, auditory, olfactory, etc. we must have a method of identifying information as being of one sensory kind or another. We may achieve this via a *modular* structure to sensation (Fodor, 1983). The modularity theory holds that whereas in non-synaesthetes,

audition and vision are functionally discrete, in individuals with synaesthesia a breakdown in modularity has occurred (Baron-Cohen *et al*., 1993). The consequence of this, in the case of colored-hearing synaesthesia, is that sounds have visual attributes. Testing the modularity theory is a challenge for future research.

RELEVANCE OF SYNAESTHESIA FOR COGNITIVE SCIENCE

Investigations of colored-hearing synaesthesia suggest that individuals with the condition are consistent in their descriptions of word–color correspondence and report similar phenomenological accounts of the condition. Further, synaesthetes appear to show different patterns of brain activation when listening to color-evoking sound stimuli. The existence of unusual neural connections between auditory and visual areas has been postulated to explain synaesthetic experience, perhaps as the result of a failure of apoptosis. Recent accounts of familiality of the condition suggest that genetic factors may sustain neonatal auditory-visual pathways. If this proves to be the case, synaesthesia may teach us how unusual wiring in the brain can lead to altered perception, and how genes may affect subjective experience.

References

Aghajanian GK (1981) In: Hoffmeister R and Stille G (eds) *Handbook of Experimental Pharmacology* **55**(2): 89–110.

Baron-Cohen S, Burt L, Laittan-Smith F, Harrison JE and Bolton P (1996) Synaesthesia: prevalence and familiality. *Perception* **25**(9): 1073–1079.

Baron-Cohen S, Harrison J, Goldstein L and Wyke M (1993) Coloured speech perception: is synaesthesia what happens when modularity breaks down? *Perception* **22**: 419–426.

Baron-Cohen S, Wyke M and Binnie C (1987) Hearing words and seeing colours: an experimental investigation of synaesthesia. *Perception* **16**: 761–767.

Calkins MW (1893) A statistical study of pseudo-chromesthesia and of mental-forms. *American Journal of Psychology* **5**: 439–466.

Critchley EMR (1994) Synaesthesia. *The Neurological Boundaries of Reality*. London, UK: Farrand Press.

Cytowic RE (1989) *Synaesthesia: A Union of the Senses*. New York, NY: Springer-Verlag.

Cytowic RE (1993) *The Man Who Tasted Shapes*. New York, NY: Putnam.

Cytowic RE and Wood F (1982) Synaesthesia: a review of major theories and their brain basis. *Brain and Cognition* **1**: 23–35.

Dehay C, Bullier J and Kennedy H (1984) Transient projections from the fronto-parietal and temporal cortex to areas 17, 18 and 19 in the kitten. *Experimental Brain Research* **57**: 208–212.

Fodor J (1983) *The Modularity of Mind*. Cambridge, MA: MIT Press.

Galton F (1883) *Inquiries into Human Faculty and Its Development*. London, UK: Dent & Sons.

Gray J, Williams S, Nunn J and Baron-Cohen S (1997) Possible implications of synaesthesia for the hard question of consciousness. In: Baron-Cohen S and Harrison JE (eds) *Synaesthesia: Classic and Contemporary Readings*. Oxford, UK: Blackwell.

Graziano MSA, Yap GS and Gross CG (1994) Coding of visual space by premotor neurons. *Science* **266**(5187): 1054–1057.

Jacobs L, Karpik A, Bozian D and Gøthgen S (1981) Auditory-visual synesthesia: sound induced photisms. *Archives of Neurology* **38**: 211–216.

Kennedy H, Batardiere A, Dehay C and Barone P (1997) Synaesthesia: implications for developmental neurobiology. In: Baron-Cohen S and Harrison JE (eds) *Synaesthesia: Classic and Contemporary Readings*. Oxford, UK: Blackwell.

Kennedy H, Bullier J and Dehay C (1989) Transient projection from the superior temporal sulcus to area 17 in the newborn macaque monkey. *Proceedings of the National Academy of Science* **86**: 8093–8097.

Lewkowicz DJ and Turkewicz G (1980) Cross-modal equivalence in early infancy: auditory-visual intensity matching. *Developmental Psychology* **16**(6): 597–607.

Marks L (1975) On colored-hearing synesthesia: cross-modal translations of sensory dimensions. *Psychological Bulletin* **82**(3): 303–331.

Marks LE (1982a) Bright sneezes and dark coughs, loud sunlight and soft moonlight. *Journal of Experimental Psychology: Human Perception and Performance* **8**(2): 177–193.

Marks LE (1982b) Synesthetic perception and poetic metaphor. *Journal of Experimental Psychology: Human Perception and Performance* **8**(1): 15–23.

Marks LE (1987) On cross-modal similarity: auditory-visual interactions in speeded discrimination. *Journal of Experimental Psychology* **13**(3): 384–394.

Maurer D (1993) Neonatal synaesthesia: implications for the processing of speech and faces. In: de Boysson-Bardies B, de Schonen S, Jusczyk P, McNeilage P and Morton J (eds) *Developmental Neurocognition: Speech and Face Processing in the First Year of Life*. Dordrecht, Netherlands: Kluwer Academic Publishers.

Meltzoff AN and Borton RW (1979) Intermodal matching by human neonates. *Nature* **282**: 403–404.

Motluk A (1994) The sweet smell of purple. *New Scientist* **143**: 32–37.

Neville HB (1993) In: de Boysson-Bardies B, de Schonen S, Jusczyk P, McNeilage P and Morton J (eds) *Developmental Neurocognition: Speech and Face Processing in the First Year of Life*. Dordrecht, Netherlands: Kluwer Academic Publishers.

Paulesu E, Harrison J, Baron-Cohen S *et al*. (1995) The physiology of coloured hearing. *Brain* **118**: 661–676.

Rang HP and Dale MM (1987) *Pharmacology*. Edinburgh, UK: Churchill Livingstone.
Rizzo M and Eslinger PJ (1989) Colored hearing synaesthesia: an investigation of neural factors. *Neurology* **39**: 781–784.
Sadato N, Pascual-Leone A, Grafman J, Ibanez V and Deiber MP (1996) Activation of the primary visual-cortex by Braille reading in blind subjects. *Nature* **380** (6574): 526–528.
Vernon PE (1930) Synaesthesia in music. *Psyche* **10**: 22–40.

Further Reading

Baron-Cohen S and Harrison JE (eds) (1997) *Synaesthesia: Classic and Contemporary Readings*. Oxford, UK: Blackwell.
Halligan PW, Hunt M, Marshall JC and Wade DT (1996) When seeing is feeling – acquired synaesthesia or phantom touch. *Neurocase* **2**(1): 21–29.
Honig MG and Hume RI (1989) Dil and dio – versatile fluorescent dyes for neuronal labeling and pathway tracing. *Trends In Neurosciences* **12**(9): 333.
Krohn WO (1893) Pseudo-chromesthesia, or the association of colors with words, letters and sounds. *American Journal of Psychology* **5**: 20–39.
Paulesu E and Frith C (1997) *The neurobiology of synaesthesia*. In: Baron-Cohen S and Harrison JE (eds) *Synaesthesia: Classic and Contemporary Readings*. Oxford, UK: Blackwell.
Ramachandran VS and Rogers-Ramachandran D (1996) Synaesthesia in phantom limbs induced with mirrors. *Proceedings of the Royal Society of London Series B – Biological Sciences* **263**(1369): 377–386.
Starr F (1893) Note on color-hearing. *American Journal of Psychology* **51**: 416–418.
Zellner DA and Kautz MA (1990) Color affects perceived odor intensity. *Journal of Experimental Psychology* **16**(2): 391–397.

Synapse

Intermediate article

Andrew Matus, Friedrich Miescher Institute, Basel, Switzerland
Michael Frotscher, University of Freiburg, Freiburg, Germany

CONTENTS

Synapses are specialized structures in neuronal circuits where signals are transmitted from one nerve cell to the next. Synaptic plasticity, involving changes in the efficiency of signal transmission and rearrangement of connections between nerve cells, is thought to underlie brain learning and memory.

INTRODUCTION

Information entering the nervous system through the sense organs is processed by vast arrays of neural circuits where it is progressively transformed into the coordinated muscle movements that make up behavior. At the same time, memory traces are laid down within these same circuits allowing animals to modify their behavior based on past experience. The function of these circuits depends on specific patterns of neuronal connections made by synapses and it is their properties and organization that lie at the heart of nervous system function.

The concept of the synapse was introduced at the end of the nineteenth century by the English physiologist Charles Sherrington, and was based on a combination of ideas from physiology and anatomy. Crucial in its inception was Sherrington's observation that reflex activity in the spinal cord always travels from the sensory fibers to the motor nerves and never in the reverse direction. This suggested the existence of a valve-like function somewhere within the reflex circuit that guaranteed the unidirectional transfer of excitation. Another key insight came from the Spanish anatomist Santiago Ramón y Cajal who argued persuasively that neuronal circuits are not continuous, as had been previously widely thought, but are composed of individual nerve cells whose axonal processes terminate in 'free' endings that are in close