



Editorial

‘Special Cases’: Neural Mechanisms and Individual Differences in Synaesthesia

The healthy ‘special case’ in neuropsychology!

Synaesthesia (Galton, 1883) is a condition in which a particular stimulus (e.g., seeing the letter R) evokes a particular additional sensation (e.g., a deep purple colour). Synaesthesia is automatic in the sense that the cross-sensations are fast and seemingly effortless, and highly consistent as the same associations persist from early childhood. Importantly, synaesthesia is found unrelated to psychological, psychiatric, or neurological ‘illness’, or to substance abuse (Baron-Cohen, Wyke, & Binnie, 1987; Rich, Bradshaw, & Mattingley, 2005). Prevalence of synaesthesia is estimated to be between 1 and 5 percent (Simner *et al.*, 2006).

Recent years have seen a sharp rise in the number of publications on synaesthesia, including publications in top journals as ‘Nature’ and ‘Nature Neuroscience’. There is a growing interest in synaesthesia not only within, but also outside of the scientific community. Examples are documentaries on television, interviews on the topic of synaesthesia in the media, and the popularity of books on synaesthesia (e.g. ‘Born on a Blue Day’ by Tammiet, 2006). One reason for this increased interest is that research has been able to prove that synaesthesia is a real condition (Baron-Cohen *et al.*, 1987; Dixon, Smilek, Cudahy, & Merikle, 2000; Mattingley, Rich, Yelland, & Bradshaw, 2001). It has clear behavioural and biological characteristics that sets it apart from ‘normal’ associations, including perceptual nature of the synaesthetic experience (Palmeri, Blake, Marois, Flanery, & Whetsell, 2002; Ramachandran & Hubbard, 2001a; Smilek, Dixon, Cudahy, & Merikle, 2001) structural differences between the brains of synaesthetes and non-synaesthetes (Hänggi, Beeli, Oechslin, & Jäncke, 2008; Jäncke, Beeli, Eulig, & Hänggi, 2009; Rouw & Scholte, 2007; Rouw & Scholte, 2010) and evidence for a genetic predisposition to having synaesthesia (Asher *et al.*, 2009; Tomson *et al.*, 2011).

Synaesthesia is important to study not only because it is an interesting topic in its own right. The unusual experiences of synaesthetes provide an extraordinary opportunity to address some of the most hotly debated questions in the field of neuroscience, including what are the mechanisms behind cross-modal sensory integration, how can a conscious sensory experiences arise in the absence of the appropriate external stimulus, and what is the neural basis of perceptual awareness. A very different factor that has pushed forward research on synaesthesia is the availability of exciting new technology. These exciting developments have provided us with new knowledge on synaesthesia. However, the strong increase of knowledge is resulting from different types of studies, from different

perspectives and using different methodologies (e.g. transcranial magnetic stimulation (TMS), electroencephalogram (EEG), voxel-based morphometry (VBM), diffusion tensor imaging (DTI), pharmacology). This makes it increasingly difficult to integrate current findings into a single interpretation.

Given these developments, the time seems ripe for a Special Issue on synaesthesia. This Special Issue is organized around two themes that are central in today's discussions in the field of synaesthesia research. They are (1) the (biological) mechanisms underlying synaesthesia and (2) individual differences. The Special Issue provides a comprehensible and integrated cross-section of current work in the field, of broad interest to the whole field of cognitive neuropsychology.

The contributors to this Special Issue are leading synaesthesia researchers with a particular interest and expertise in one or both of the themes. The *Journal of Neuropsychology* is the appropriate journal for this Special Issue. First, neuropsychology is the classical approach to linking deviations in behaviour to variations in brain structure and brain functioning. Thus, relating behavioural to biological properties of these 'special' individuals fits in the rich tradition of neuropsychological research. Second, neuropsychology has taught us how to understand and describe (categorize) deviant behaviour. How to categorize the individual differences in the range of 'special' behaviour shown by synaesthetes is a key question in the field. The two themes of this Special Issue thus reflect the current developments in the field and closely correspond to the scope of the *Journal of Neuropsychology*. Below, there is a summary of the main conclusions in this Special Issue, as well as placing these in the context of general developments in the field.

What are the biological mechanisms underlying synaesthesia?

Moving from a focus on one particular brain region into defining networks of brain regions

Two conclusions emerge from this Special Issue. First, the answer to this question shifts from relating one particular brain area to a particular (synaesthetic) function, into defining a *network* of several brain areas involved in this function. Rather than relating a particular type of synaesthetic experience to activation of a particular sensory cortex, in this Special Issue progress is made in designing models where multiple brain areas are instead the focus of attention. Specht & Laeng (2011, in this issue) applied independent component analysis (ICA) on fMRI data from grapheme-colour synaesthetes and matched controls, to study networks of brain areas involved in synaesthesia. A review of neuroimaging studies on synaesthesia (Rouw, Scholte, & Colizoli, 2011, in this issue) concludes that a network of brain areas rather than a single brain region underlies synaesthesia. The review article describes six different brain regions that emerge from the literature. While not all studies will come to this particular number of brain regions, the trend to think in a network of brain areas rather than isolated brain areas is generally present. In this Special Issue, an updated version (Hubbard, Brang, & Ramachandran, 2011) is presented of a key model in synaesthesia literature, the 'cross-activation model' (Ramachandran & Hubbard, 2001a, b). One of the modifications to the model is to 'zoom out', from a focus on a particular brain region of cross-activation, to including other brain areas crucial to synaesthesia. In particular, the cross-activation model of grapheme-colour synaesthesia is extended to include parietal cortex involved in synaesthetic binding. In support of this modification, Jäncke and Langer (2011, in this issue) found that the left-sided parietal lobe is a strong hub region, in addition to the relevant (auditory cortex)

sensory brain area. A hub is a region with strong interconnections to other regions. This article takes an important step by investigation connectivity or brain networks, rather than looking at activation in singular brain areas. Jäncke and Langer (2011) present functional brain networks of synaesthetes, based on data of resting state EEG activity. Graph theoretical analysis showed different synaesthesia hubs, proposed to be involved in different types of functions.

This brings us to the second conclusion. More and more, it is possible to decipher how these (networks of) brain areas relate to different aspects or different functions of synaesthesia. While this is a 'work in progress', this Special Issue allows a step forward in gaining insight in these relationships. Looking at these and other recent studies the following functions emerge. First, certain brain regions are clearly related to the *sensory experience* itself. Jones *et al.* (2011, in this issue) found insula activation when synaesthetes view words that elicit taste with an emotional valence. Specht and Laeng (2011, in this issue) found a 'perceptual network', involving posterior temporal, inferior occipital and right prefrontal brain areas. The 'cross-activation' model proposes increased connectivity and activation from one to another brain area, positioned at the corresponding sensory brain region. Furthermore, different *aspects of the experience* might also change properties of the brain networks. Jones *et al.* found increased insula activation related to the emotional valence of a word, while intensity of the synaesthesia was correlated with medial parietal activity. Amin *et al.* (2011, in this issue) found precuneus activation in a synaesthete who personifies graphemes and related this to general aspects of synaesthesia; mental imagery and/or self-referential processing abilities. A very different function of synaesthesia is the *attentional or binding* aspect. The analysis from Specht and Laeng also revealed a fronto-parietal 'attention' network. As described previously, the updated 'cross-activation' model includes a parietal region and relates this to synaesthetic binding, and an important conclusion by Jäncke and Langer (2011, in this issue) is that the left-sided parietal lobe is a strong hub in the synaesthetic brain. Other functions might relate to different networks of brain areas. For example, the study from Specht and Laeng found a third network involving medial structures such as anterior cingulate cortex, thalamus, precuneus, and the insular cortex. The insula is one of the six regions mentioned in our review (Rouw *et al.*, 2011). Precuneus and insula activation are reported in the study of grapheme personification by Amin *et al.*, and in the study of lexical-gustatory synaesthesia by Jones *et al.* It is not yet clear what is the best interpretation of these results. However, these interesting overlapping findings support the notion that different functions in synaesthesia can relate to different (networks of) brain areas. Future research will further identify these specific functions.

While a review of recent research is beyond the scope of this article, these findings and the emerging two conclusions are in line with reports in recent synaesthesia literature. Examples are publications on brain network topology in synaesthesia (Hängi, Wotruba, & Jäncke, 2011) and the development of 'synaesthetic' brain networks (Mitchell, 2011).

Individual differences

Categorical versus graded differences between synaesthetes and non-synaesthetes

The second theme of the Special Issue is individual differences. This theme refers to the question whether synaesthetes are simply at one extreme of normal individual differences in (sensory) experiences, or whether synaesthetes are categorically or qualitatively

different from non-synaesthetes. It also refers to the insight that synaesthesia cannot be understood unless taking into account individual differences between synaesthetes.

As noted previously, synaesthetes can be viewed as 'special case' studies. One remarkable and unusual aspect of these neuropsychological 'cases' is that the synaesthesia is part of their normal life without interrupting it. In fact, synaesthetes generally experience their condition as useful and even pleasant (e.g., synaesthetes have improved memory functions, Smilek, Dixon, Cudahy, & Merikle, 2002; Yaro & Ward, 2007). synaesthesia therefore provides both a contribution to and a contrast with *clinical* studies on perceptual sensory awareness and integration. This is also the reason why many neuropsychologists will not know of this condition. Few synaesthetes will talk about their synaesthesia to a clinician. Synaesthetes often report that their synaesthesia is 'just there'. Unless the situation requires it, there are no particular reasons to talk about it.

In the literature, diverging answers are given to the question in what manner synaesthetes differ from non-synaesthetes. This ranges from a qualitatively and categorically different state on one hand, to assuming that synaesthesia only reflects using the extreme end of 'normal' mechanisms on the other hand.

In this Special Issue, Simner, Gärtner, and Taylor (2011) shed light on this issue in a group study of synaesthetes where sequenced units (letters and numbers) have a personality or gender. Asking non-synaesthetes to also link personalities to letters revealed that non-synaesthetes and synaesthetes use the same underlying rules. For example, high-frequency letters were linked with high agreeable personality. Synaesthetes do however, differ from non-synaesthetes in other aspects; the phenomenology of their reports, the depth of their personality associations, as well as the consistency of those associations over time, is different. Jonas, Taylor, Hutton, Weiss, and Ward (2011) document, for the first time, the characteristics of synaesthetic alphabet forms. These visuo-spatial representations of the alphabet may be as common as other types of sequence-space synaesthesia. The study also examines how the alphabet forms relate to implicit spatial associations in the general population. Again, there are similarities; in particular, the 'alphabet song' chunking of the forms shows how the visuo-spatial characteristics are related to general ideas of verbal sequence (learned early in life). There are also differences, as letters can act as attentional cues to left/right space in synaesthetes with alphabet forms (measured by saccades), but not in non-synaesthetes. A different type of sequence-space synaesthesia was studied by Brang, Teuscher, Miller, Ramachandran, and Coulson (2011, this issue). Time-space synaesthetes report that time units (e.g. months) have a spatial arrangement. Brang *et al.* show how the calendars are mediated by handedness; a counter-clockwise arrangement tends to be found in left-handed synaesthetes, while right-handed synaesthetes report clockwise arrangements. Presenting experiments with calendar arrangements to non-synaesthetes shows a similar relationship between handedness and preferred spatial arrangement. The authors propose that these biases in synaesthetes and non-synaesthetes are mediated by similar mechanisms, uncovering the graded nature of synaesthetic associations. The controversy is also found in neuroimaging studies. Functional and structural brain differences are found between synaesthetes and non-synaesthetes, but shared mechanisms are also reported. In this issue, Specht and Laeng (2011) show that the neural substrate that is known to support the experience of physical colours also supports the experience of synaesthetic colours.

Taken together these findings might seem conflicting, including both similarities and differences between synaesthetes and non-synaesthetes. One way to possibly understand

this is by following a ‘trait-type’ distinction. Family studies as performed by Barnett *et al.* (2008) and Rich *et al.* (2005) show how having synaesthesia is running in families, but there are no familial trends in having a particular type of synaesthesia. Accordingly, we (Rouw *et al.*, 2011) propose that synaesthetes are different in all aspects that are related to having (the trait) synaesthesia. In contrast, synaesthetes are similar to non-synaesthetes in what shapes the particular type of association. Simner *et al.* (2011) note how the phenomenology between synaesthetes and non-synaesthetes is different. Similarly, Jonas *et al.* (2011) note how only for synaesthetes the letters stand out as an attentional cue. These differences reflect differences in the nature of the experience; this is one of the defining characteristics of having the trait synaesthesia. In contrast, the types of associations are shaped by environment (one is not born with an R, let alone a red R). The environment is shared between synaesthetes and the non-synaesthetes, and will give the same bias to these two types of associations. Of course, this ‘trait-type’ model is just one interpretation of the controversy. The studies presented in this Special Issue provide a step forward in deciphering which mechanisms are shared and which are different between synaesthetes and non-synaesthetes.

As important as the previous topic, is the topic of understanding individual differences *within* a group of synaesthetes. This difference between types of synaesthesia can even take place within an individual, an important insight provided by the study of Jarick, Jensen, Dixon, & Smilek (2011, in this issue). Synaesthete L will quickly and automatically change mental viewpoint (perspective) of her synaesthetic time-space line, depending on whether the month name is presented visually or aurally. This Special Issue presents a broad variety of types of synaesthesia. These include experiencing sequenced units as letters or numbers with a personality or gender (Simner *et al.*, 2011) and grapheme personification (Amin *et al.*, 2011); experiencing flavour while reading, hearing, or imagining words (lexical-gustatory synaesthesia; Jones *et al.*, 2011); visual-spatial representation of the alphabet (Jonas *et al.*, 2011) and the calendar (Brang *et al.*, 2011; Jarick *et al.*, 2011); and seeing colours while seeing or hearing letters and numbers (grapheme-colour synaesthesia and coloured hearing synaesthesia, Hubbard, Brang, & Ramachandran, 2011; Jäncke & Langer, 2011; Rouw *et al.*, 2011; Specht & Laeng, 2011).

The study from Novich, Cheng, and Eagleman (2011, in this issue) provides important insight in the relationships between different types of synaesthesia. Based on data of 19.133 online participants, the authors examined which synaesthesia types tend to co-occur. The analyses converged on five distinct groupings of types of synaesthesia. Based on their analyses, the authors suggest that coloured sequence, coloured music, non-visual sequela, spatial sequence, and coloured sensations are five distinct groups with independent probabilities of expression. This study thus shows how differences between synaesthetes can be understood. The authors suggest that these may possibly be related to distinct mechanisms and different genetic bases.

Romke Rouw (University of Amsterdam, The Netherlands)

References

- Amin, M., Olu-Lafe, O., Claessen, L. E., Sobczak-Edmans, M., Ward, J., Williams, A. L., & Sagiv, N. (2011). Understanding grapheme personification: A social synaesthesia? *Journal of Neuropsychology*, 5, 255–282. doi:10.1111/j.1748-6653.2011.02016.x
- Asher, J. E., Lamb, J. A., Brocklebank, D., Cazier, J. B., Maestrini, E., Addis, L., *et al.* (2009). A whole-genome scan and fine-mapping linkage study of auditory-visual synesthesia reveals evidence

- of linkage to chromosomes 2q24, 5q33, 6p12, and 12p12. *The American Journal of Human Genetics*, 84(2), 279–285.
- Barnett, K. J., Finucane, C., Asher, J. E., Bargary, G., Corvin, A. P., Newell, F. N., & Mitchell, K. J. (2008). Familial patterns and the origins of individual differences in synaesthesia. *Cognition*, 106(2), 871–893.
- Baron-Cohen, S., Wyke, M. A., & Binnie, C. (1987). Hearing words and seeing colours, an experimental investigation. *Perception*, 16(6), 761–767.
- Brang, D., Teuscher, U., Miller, L. E., Ramachandran, V. S., & Coulson, S. (2011). Handedness and calendar orientations in time-space synaesthesia. *Journal of Neuropsychology*, 5, 323–332. doi:10.1111/j.1748-6653.2011.02012.x
- Dixon, M. J., Smilek, D., Cudahy, C., & Merikle, P. M. (2000). Five plus two equals yellow: Mental arithmetic in people with synaesthesia is not coloured by visual experience. *Nature*, 406(6794), 365.
- Galton, F. (1883). Colour associations. In S. Baron-Cohen & J. E. Harrison (Eds.), *Synaesthesia: Classic and contemporary readings* (1997; pp. 43–48). Oxford, England: Blackwell.
- Hänggi, J., Beeli, G., Oechslin, M. S., & Jäncke, L. (2008). The multiple synaesthete ES—Neuroanatomical basis of interval-taste and tone-colour synaesthesia. *Neuroimage*, 43(2), 192–203.
- Hänggi, J., Wotruba, D., Jäncke, L. (2011). Globally altered structural brain network topology in grapheme-color synesthesia. *Journal of Neuroscience*, 31(15), 5816–5828.
- Hubbard, E. M., Brang, D., & Ramachandran, V. S. (2011). The cross-activation theory at 10. *Journal of Neuropsychology*, 5, 152–177. doi:10.1111/j.1748-6653.2011.02014.x
- Jäncke, L., Beeli, G., Eulig, C., & Hänggi, J. (2009). The neuroanatomy of grapheme-color synesthesia. *European Journal of Neuroscience*, 29(6), 1287–1293.
- Jäncke, L., & Langer, N. (2011). A strong parietal hub in the *small-world* network of coloured-hearing synaesthetes during resting state EEG. *Journal of Neuropsychology*, 5, 178–202. doi:10.1111/j.1748-6653.2011.02004.x
- Jarick, M., Jensen, C., Dixon, M. J., & Smilek, D. (2011). The automaticity of vantage point shifts within a synaesthetes' spatial calendar. *Journal of Neuropsychology*, 5, 333–352. doi:10.1111/j.1748-6653.2011.02011.x
- Jonas, C. N., Taylor, A. J. G., Hutton, S., Weiss, P. H., & Ward, J. (2011). Visuo-spatial representations of the alphabet in synaesthetes and non-synaesthetes. *Journal of Neuropsychology*, 5, 302–322. doi:10.1111/j.1748-6653.2011.02010.x
- Jones, C. L., Gray, M. A., Minati, L., Simner, J., Critchley, H. D., & Ward, J. (2011). The neural basis of illusory gustatory sensations: Two rare cases of lexical-gustatory synaesthesia. *Journal of Neuropsychology*, 5, 243–254. doi:10.1111/j.1748-6653.2011.02013.x
- Mattingley, J. B., Rich, A. N., Yelland, G., & Bradshaw, J. L. (2001). Unconscious priming eliminates automatic binding of colour and alphanumeric form in synaesthesia. *Nature*, 410(6828), 580–582.
- Mitchell, K. J. (2011). Curiouser and curiouser: Genetic disorders of cortical specialization. *Current Opinion in Genetics & Development*, 21, 1–7.
- Novich, S., Cheng, S., & Eagleman, D. M. (2011). Is synaesthesia one condition or many? A large-scale analysis reveals subgroups. *Journal of Neuropsychology*, 5, 353–371. doi:10.1111/j.1748-6653.2011.02015.x
- Palmeri, T. J., Blake, R. B., Marois, R., Flanery, M. A., & Whetsell, W. O. (2002). The perceptual reality of synesthetic color. *Proceedings of the National Academy of Sciences of the United States of America*, 99, 4127–4131.
- Ramachandran, V. S., & Hubbard, E. M. (2001a). Psychophysical investigations into the neural basis of synaesthesia. *Proceedings of the Royal Society Biological Sciences Series B*, 268(1470), 979–983.
- Ramachandran, V. S., & Hubbard, E. M. (2001b). Synaesthesia: A window into perception, thought and language. *Journal of Consciousness Studies*, 8(12), 3–34.

- 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-colour associations. *Cognition*, *98*(1), 53–84.
- Rouw, R., & Scholte, H. S. (2007). Increased structural connectivity in grapheme-color synesthesia. *Nature Neuroscience*, *10*(6), 792–797.
- Rouw, R., & Scholte, H. S. (2010). Neural basis of individual differences in synesthetic experiences. *Journal of Neuroscience*, *30*(18), 6205–6213.
- Rouw, R., Scholte, H. S., & Colizoli, O. (2011). Brain areas involved in synaesthesia: A review. *Journal of Neuropsychology*, *5*, 214–242. doi:10.1111/j.1748-6653.2011.02006.x
- Simner, J., Gärtner, O., & Taylor, M. D. (2011). Cross-modal personality attributions in synaesthetes and non-synaesthetes. *Journal of Neuropsychology*, *5*, 283–301. doi:10.1111/j.1748-6653.2011.02009.x
- Simner, J., Mulvenna, C., Sagiv, N., Tsakanikos, E., Witherby, S. A., Fraser, C., . . . Ward, J. (2006). Synaesthesia: The prevalence of atypical cross-modal experiences. *Perception*, *35*(8), 1024–1033.
- Smilek, D., Dixon, M. J., Cudahy, C., & Merikle, P. M. (2001). Synaesthetic photisms influence visual perception. *Journal of Cognitive Neuroscience*, *13*(7), 930–936.
- Smilek, D., Dixon, M. J., Cudahy, C., & Merikle, P. M. (2002). Synesthetic color experiences influence memory. *Psychological Science*, *13*, 548–555.
- Specht, K., & Laeng, B. (2011). An independent component analysis of fMRI data of grapheme-colour synaesthesia. *Journal of Neuropsychology*, *5*, 203–213. doi:10.1111/j.1748-6653.2011.02008.x
- Tammet, D. (2006). *Born on a blue day*. London: Hodder & Stoughton.
- Tomson, S. N., Avidan, N., Lee, K., Sarma, A. K., Tushe, R., Milewicz, D. M., . . . Eagleman, D. M. (2011). The genetics of colored sequence synesthesia: Suggestive evidence of linkage to 16q and genetic heterogeneity for the condition. *Behavioural Brain Research*, *223*, 48–52.
- Yaro, C., & Ward, J. (2007). Searching for Shereshevskii: What is superior about the memory of synaesthetes? *Quarterly Journal of Experimental Psychology*, *60*, 681–695.

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