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Article (Accepted Version)

Simner, J, Rehme, M K, Carmichael, D A, Bastin, M E, Sprooten, E, McIntosh, A M, Lawrie, S M and Zedler, M (2016) Social responsiveness to inanimate entities: altered white matter in a ‘social synaesthesia’. *Neuropsychologia*, 91. pp. 282-289. ISSN 0028-3932

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Social responsiveness to inanimate entities: Altered white matter in a ‘social synaesthesia’

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ABSTRACT

Judgments about personalities and social traits can be made by relatively brief exposure to animate living things. Here we show that unusual architecture in the microstructure of the human brain is related to atypical mental projections of personality and social structure onto things that are neither living nor animate. Our participants experience automatic, life-long and consistent crossmodal associations between language sequences (e.g., letters, numbers and days) and complex personifications (e.g., A is a businessman; 7 a good-natured woman). Participants with this ‘Ordinal Linguistic Personification’ (Simner & Hubbard, 2006) which we describe here as a form of social synaesthesia, showed lower fractional anisotropy (FA) values in five clusters at whole-brain significance, compared with non-synaesthetes (in the pre-postcentral gyrus/ dorsal corticospinal tract, left superior corona radiata, and the genu, body and left side of the corpus callosum). We found no regions of the brain with increased FA in synaesthetes. A number of these regions with reduced FA play a role in social responsiveness, and our study is the first to show that unusual differences in white matter microstructure in these regions is associated with compelling feelings of social cohesion and personality towards non-animate entities. We show too that altered patterns of connectivity known to typify synaesthesia are not limited to variants involving a ‘merging of the senses’, but also extend to

what might be thought of as a cogno-social variant of synaesthesia, linking language and personality attributes in this surprising way.

Key words: Synaesthesia, DTI, sequence-personality, personification, white matter

HIGHLIGHTS

- Atypical social attributions linked to altered white matter microstructure
- FA was reduced in 5 clusters involved in processing sequences and social relationships
- Neural markers of synaesthesia are not limited to sensory variants of the condition

1. INTRODUCTION

The human brain is poised to readily perceive social intention in the complex human environment in which we live. We are able to interpret bodily gestures, facial expressions, the spoken word, and many other sources of information as key to revealing the underlying personality and social makeup of those around us. Such judgements can be made even when the human quality of the stimulus is degraded in some way, for example when observing point-light walkers in the dark (Heberlein & Saxe, 2005). Indeed, judgements can even be made when there is no human stimulus at all: the famous Heider-Simmel animations (Heider & Simmel, 1944) show that geometric shapes, if acting sufficiently human-like -- and that means moving towards and away from each other in specific ways -- can be imbued with social intentions of love, menace, celebration and so on. In such cases, social judgements are possible only because there are human qualities inherent in the stimulus or in the way it moves, no matter how stripped back. In the current study we show that that unusual architecture in the microstructure of the human brain is linked to atypical personality and social projections onto inanimate entities, even if they have no human-like qualities whatsoever.

In this study we tested a group of participants with the unusual experience of *Ordinal Linguistic Personification* (OLP; Simner & Hubbard, 2006). People with OLP see letters, numbers and other types

of ordered language units (e.g., days of the week) as having complex personalities and social orders. For example, an individual with OLP might experience the letter A as being a middle-aged businessman, or the number 7 as a naïve young girl. These associations are lifelong intuitively held beliefs, and have been reported in the literature for at least the last 120 years (eg., Calkins, 1893; Flournoy, 1893). Contemporary interest in OLP has reemerged sporadically in the last decade (Amin et al., 2011; Simner, Gartner, & Mills, 2011; Simner & Hubbard, 2006; Simner & Holenstein, 2007) but despite behavioural studies validating the consistency and automaticity of these associations (e.g., Simner & Holenstein, 2007) very little progress has been made understanding the neural architecture driving them. This architecture does not appear to involve regions tied to empathy for example, since, despite their unusual personality attributions, people with OLP score no higher than average on questionnaire such as the Empathy quotient (Baron-Cohen & Wheelwright, 2004). Instead we suggest that at the heart of this OLP architecture may be differences in regions involved in social responsiveness -- the ability to recognize emotional and interpersonal signals from others. OLP personifications are felt to engage socially (e.g., G and H gossip together, Simner & Hubbard, 2006) and hold social/emotional relationships not only among themselves (8 is dating 9 but loves 7; Simner & Holenstein, 2007) but also with respect to the OLP individual who experiences them ("Three is a real jerk... he'll manipulate you and stab you in the back..." Smilek et al., 2007, pg. 981). They can form a range of social groups including families and neighbourhoods (e.g., J is the mother of I; Simner & Hubbard, 2006; M and N are neighbours, Simner & Holenstein, 2007) and they therefore appear to derive from a type of atypical social attribution process, and this might lead us to expect altered structure in regions involved in social processing (see below)..

To understand what type of altered neural structure could be involved, we might also look to other types of lifelong, atypical, automatic cross-modal associations. In these terms, OLP could be categorised as a form of developmental synaesthesia. Synaesthesia is a genetically linked condition

(Asher et al., 2009; Tomson et al., 2011) in which every-day stimuli trigger unusual secondary associations. Archetypal manifestations of synaesthesia include cases where two senses are 'merged' in some way, such as when music triggers visual perceptions of colour (e.g., Ward, Huckstep & Tsakanikos, 2006) or where tastes trigger tactile sensations of shape (e.g., Cytowic, 1993). However, the neural conditions giving rise to synaesthesia (e.g., atypical white-matter coherence; see below) could in theory be found in *non*-sensory variants, including the example under investigation here. Like more typical synaesthesias, OLP automatically and developmentally pairs two otherwise unrelated modalities, and is triggered by the most common triggers for synaesthesia in general (i.e., ordered sequences; see Simner et al., 2006). It has therefore been suggested that OLP is a 'cognitive' or 'social' variant of synaesthesia (e.g., Simner & Holenstien, 2007; Amin et al., 2011) which we label henceforth as 'sequence-personality synaesthesia'. Here we present a structural imaging study of a group of individuals with this form of OLP/ sequence-personality synaesthesia, to determine whether they show similar changes in brain structure that have been found in other variants of synaesthesia more broadly.

Here we examine the structural neural basis of synaesthesia using the method of *diffusion tensor MRI* (DTI), which provides information about white matter microstructure by tracking the movement of water molecules in the brain. A commonly used metric derived from DTI is *fractional anisotropy* (FA), which reflects the extent to which water molecule movement is restricted in directions perpendicular to white matter fibres, relative to directions parallel to the fibres (on a scale from 0 to 1). The lower the FA value, the greater extent to which water molecules are free to diffuse in any direction. The directional preference of the diffusion of water molecules in white matter, as indexed by FA, can be influenced by a number of factors including axonal diameter, density of fibre bundles, degree of myelination and permeability of the axonal membrane (Takahashi et al., 2002). Thus, molecules moving anisotropically (unequally in one dimension) indicate greater numbers or integrity of white

matter fibres. In the current study we use this technique to present the first FA data from the unusual experience of OLP/ sequence-personality synaesthesia.

A number of studies have previously compared FA between synaesthetes and nonsynaesthetic controls. Five of these studies were carried out using grapheme-colour synaesthetes as participants. *Grapheme-colour synaesthesia* is the automatic and lifelong association between graphemes (letters/digits) and colours, and Rouw and Scholte (2007) found increased FA in grapheme-colour synaesthetes in four brain regions they describe as: bilaterally in the superior temporal lobe, left superior parietal cortex and the right inferior temporal cortex. Recently, O'Hanlon, Newell and Mitchell (2013) also report increased FA in synaesthetes in a number of clusters; three of which were located in the right superior longitudinal fasciculus, two in the right inferior longitudinal fasciculus and two in the thalamus. Jäncke, Beeli, Eulig and Hänggi (2009) found no differences in FA between groups of synaesthetes and nonsynaesthetes in their hypothesised region of the fusiform gyrus, but did report increased FA in synaesthetes in the hippocampus, fronto-occipital fasciculus and the splenium of the corpus callosum. One additional study (Melero et al., 2013) showed increased FA in synaesthetes, but at a liberal uncorrected significance threshold of $p < 0.001$ (in left middle/inferior frontal gyrus, left cuneus, left middle occipital gyrus, left cingulate gyrus and right anterior insula). The same study also reported decreased FA in synaesthetes in the thalamus. Finally, Whitaker et al. (2014) report reduced FA in synaesthetes in a very large number of regions distributed throughout the brain, including the corpus callosum, corona radiata and the superior longitudinal fasciculus to name a few.

Studies have also been carried out examining white matter infrastructure in other forms of synaesthesia, too. Using a regions of interest analysis looking at connectivity between auditory and visual regions of the brain, Zamm, Schlaug, Eagleman and Loui (2013) studied *sound-colour synaesthetes* and found increased FA in the right inferior fronto-occipital fasciculus, a white matter

tract that connects occipital and frontal regions. In a case study of a single synaesthete with sound-colour and *sound-taste* synaesthesias, Hänggi, Beeli, Oechslin and Jäncke (2008) showed increased FA values in the primary auditory cortex, as well as structural differences in grey and white-matter in visual and gustatory regions (i.e., increases in occipital regions, and increases and decreases in insular cortex). In other words, differences have been found in structures in distributed regions including those related to both the synaesthetic *inducer* (the triggering stimulus) and the synaesthetic *concurrent* (the resultant secondary sensation; see Ward, 2013; Rouw, Scholte & Colizoli, 2011; for review), and FA has been increased and reduced relative to controls.

Although these studies cover a range of different variants, no study has yet examined whether similar alterations in white matter can be found in the rather unusual case of sequence-personality synaesthesia, a qualitatively different form of the condition whose neural basis is still largely unknown. There has been just one previous imaging study in this area, by Amin et al. (2011) who presented functional rather than structural data, and tested a single synaesthete. Amin et al. performed functional magnetic resonance imaging (fMRI) of a case-study with a relatively restricted form of sequence-personality synaesthesia in which just letters -- and only a subset of the alphabet in particular-- triggered personifications, and these personifications were limited to genders only (e.g., A might be, say, female). In their task, the synaesthete was instructed to detect repetition within lists of letters presented one-at-a-time onscreen, and materials were blocked according to whether the list contained letters that did (vs. did not) trigger synaesthesia. Compared to a group of controls, the synaesthetes showed only precuneus activation suggesting, according to the authors, some role for

networks involved in self-reflection and/or mental imagery. However, Amin et al. point out that their case-study approach requires caution when considering the absence of effects in any other areas.

In this study we present data from a group of sequence-personality synaesthetes rather than a case-study; and we tested participants who had very well developed sequence-personality synaesthesia in particular. All subjects had both genders and complex social personalities for an average of 3.1 (SD 1.4) out of four possible types of triggering sequences we questioned them about: letters, numbers, days and months (see Table 1). For example, for participant BB, the letter n is “small and timid”, while for synaesthete JH, the number 4 is “a team-player that likes being in groups”. Additionally, for synaesthete EG, Monday is “a gentle but slightly anxious character”, while August is “tired and brusque”, and so on. Although DTI studies are ideally performed on larger group sizes, the rarity of the condition under consideration here necessarily limited participation numbers. We acknowledge, like Amin et al., that small sample sizes call for caution in interpreting these findings (see also Hupé & Dojat, 2015 for discussion); however, we were able to test 12 such synaesthetes with these unusual experiences, whom we flew to our testing centre from around the UK.

Based on prior literature we hypothesise that sequence-personality synaesthetes may show increased (e.g., Rouw & Scholte, 2007) or decreased (e.g., Whitaker et al., 2014) FA in regions implicated in either the trigger or concurrent. This might include regions recruited when thinking about sequences, such as numbers (e.g., Tang, Ward, & Butterworth, 2008) or letters (e.g., Rouw & Scholte, 2007), and/or social processing regions. Candidate regions in this latter regard might be somatosensory cortices and inferior parietal and frontal regions, all implicated in social responsiveness (Adolphs, 2003; see Discussion for further details). We may also find the involvement of more widely distributed regions (e.g., Whitaker et al., 2014) implicated perhaps in parietal ‘binding’ processes (see Rouw & Scholte, 2007) or self-reflection/ imagery (e.g., Amin et al., 2011). Key however are likely to be regions that

reflect the primarily personality/social mappings that are inherent in the OLP/ sequence-personality experience. If so, this will be the first study to show that unusual architecture in the microstructure of the human brain may be related to atypical projections of social structure onto inanimate and abstract entities.

2. MATERIALS AND METHODS

Participants. We tested 12 native British participants (all female, mean age=35.6 years, SD=12.0) with the rare condition of sequence-personality synaesthesia. Table 1 shows the particular triggers for their sequence-personality synaesthesia, which were letters and/or numbers and/or days and/or months, and their synaesthetic associations were personality traits and/or genders. All participants were recruited from a database of synaesthete participants (see www.syn.sussex.ac.uk). Scanning took place in Edinburgh and matched controls were recruited from the University of Edinburgh community, who were first screened by questionnaire (see Simner et al., 2006) to ensure they did not have any form of synaesthesia. The two groups were matched for sex, age (control mean age=33.8 years; SD=9.7),

nationality, native language, handedness and level of education. Ethical approval was granted in advance of study¹.

Table 1. Manifestations of sequence-personality synaesthesia experienced by our n=12 synaesthete participants. Column 1 shows the synaesthetic inducer, and Column 2 shows the synaesthetic concurrent.

Inducer	Concurrent	AT	SG	JB	AL	CL	EG	JH	BB	GW	SM	PM	BH
Letters	gender	x	x	x	x	x	x	x	x	x	x	x	x
	personality	x	x	x	x	x	x		x	x	x	x	x
numerals	gender		x	x	x	x	x	x	x	x	x		x
	personality		x	x	x	x	x	x		x	x	x	x
Days	gender		x	x	x	x	x			x			x
	personality		x	x	x	x	x			x	x		x
Months	gender		x	x	x	x	x	x		x			x
	personality		x	x	x	x	x			x	x		x

Behavioural pretest. We first established that our synaesthetes' reports were genuine using what is recognised as the behavioural 'gold standard' test for synaesthesia (e.g., Asher et al., 2009; Rich, Bradshaw & Mattingley, 2005). This test relies on the fact that synaesthetic pairings are highly consistent over time, and in our test, we established that our synaesthetes' associations (e.g., A = good-natured woman) were consistent over at least two years. Synaesthetes were given a written questionnaire in which they described their gender and personalities to 26 letters, 10 numerals, 7 days

¹ An anonymous reviewer has asked us to comment on whether our synaesthetes as a group had numerical deficits, given that our results show a role for the corona radiata). We can confirm this was not the case. Eleven of our 12 synaesthetes completed a brief questionnaire which included the question "Do you have (or have you ever had) problems with understanding numbers and/or calculation?" to which 2 of 11 synaesthetes agreed or strongly agreed. A group of n=11 controls without synaesthesia completed the same questionnaire of which 4 out of 11 agreed. We can therefore conclude there were no *a priori* deficits in numerical abilities in our synaesthetes compared to controls. The same is true regarding allochiria (i.e., left/right confusion; 4 synaesthetes vs. 3 non-synaesthetes agreed) and regarding dyslexia/reading/writing problems (4 synaesthetes vs. 3 non-synaesthetes agreed).

and 12 months, according to the particular variant(s) of sequence-personality synaesthesia they reported (see Table 1). Synaesthetes were then given a surprise retest more than two years on average later (mean 2.2 years; SD = 1.2). In order to show that OLP synaesthetes are more consistent than controls (and therefore that measuring consistency is a valid way of identifying genuine OLP synaesthetes), thirty additional non-synaesthete behavioural controls (mean age=24.2, SD=10.0) were asked to freely associate genders and personality adjectives to the same stimuli (10 controls were given letters and numbers; 20 controls were given days and months). Controls then recalled those associations from memory after just 3 weeks (mean 22.3 days, SD=5.1). Data from these behavioural controls are reported below in Table 2.

MRI protocol. All MRI data were collected using a GE Signa LX 1.5 T (General Electric, Milwaukee, WI, USA) scanner with a self-shielding gradient set (22 mT/m maximum gradient strength) and 'birdcage' quadrature head coil. The MRI examination consisted of a standard fast spin-echo T₂-weighted sequence, a fast spoiled gradient-echo T₁-weighted volume, and a whole brain DTI protocol. In the latter, a single-shot pulsed gradient spin-echo echo-planar imaging (EPI) sequence was used to acquire sets of axial images (b = 0 and 1000 s/mm²) with diffusion gradients applied sequentially along 64 non-collinear directions arranged uniformly in space. Fifty three contiguous axial slice locations were imaged and, in addition to the 64 diffusion-weighted EPI volumes, seven non-diffusion weighted (b₀) volumes were also acquired (TE=13,5ms, TR=17sec, FOV= 24.0x24.0 cm, slice thickness = 2.5 mm, matrix =96 x 96 (zero filled to 128 x 128), voxel dimension = 1.875 x 1.875 x 2.5mm, flip angle 90 deg.). A single average was collected and the DTI acquisition took approximately 10 minutes. The whole examination took approximately 30 minutes.

Image processing. All DICOM images were converted into NIfTI format (<http://nifti.nimh.nih.gov>). Using FSL FLIRT (<http://www.fmrib.ox.ac.uk/fsl>), random subject motion and eddy current induced

artefacts were removed from the brain-extracted (FSL BET) DTI data by registering the diffusion-weighted to the first b0 volume. The diffusion tensor (**D**) was calculated in each voxel from the signal intensities in the component EPI data using FSL DTIFIT. FA maps for every subject were generated on a voxel-by-voxel basis from the sorted eigenvalues of **D**, resulting in a series of skull-stripped FA for further analysis.

Tract based spatial statistics. The FA data were analysed using Tract-Based Spatial Statistics (TBSS; Smith et al., 2006) according to standard FSL procedures (<http://www.fmrib.ox.ac.uk/fsl>). Firstly, the FA volume for each subject was linearly and non-linearly registered to the standard-space FMRIB58_FA template, and a mean of all registered FA volumes calculated. A mean white matter skeleton was then created by searching for the maximum FA values in directions perpendicular to the local tract direction in the mean FA map, with predominantly non-white matter voxels excluded by applying an FA threshold of 0.2. Next, for each subject's FA volume, the maximum voxel perpendicular to the local skeleton direction was projected onto the skeleton at each point. This produces an FA skeleton for each subject, assumed to contain anatomically corresponding centres of the major white matter structures. Between-group differences in FA (both synaesthetes > controls and controls > synaesthetes t-tests) fully corrected for multiple comparisons across space were assessed using the standard approach of Threshold-Free Cluster Enhancement (TFCE) in FSL Randomise using 5000 permutations (<http://fsl.fmrib.ox.ac.uk/fsl/fslwiki/TBSS/UserGuide>; Smith and Nichols, 2009; Winkler et al., 2014). Significant clusters were determined by ensuring family-wise error rates (FWE; based on 5000 permutations) below $p < 0.05$ across the entire white matter skeleton.

3. RESULTS

3.1 Behavioural results. The two subject groups, synaesthetes and behavioural controls, performed significantly differently in a diagnostic tests of synaesthesia. [We conducted 8 consistency tests, and](#)

participants' responses were coded by the first author as 1 or 0 where 1 is a consistent response over time (e.g., A=Male time 1, Male time 2) and 0 an inconsistent response (e.g., A=Male time 1, Female time 2 OR no response time 2). Consistency scores were then converted to percentages and compared across groups. Despite retesting synaesthetes over a considerably longer time interval of >2 years, their mean overall consistency (73.8%; SD = 11.2) across all types of sequence-personality synaesthesia we tested (see Table 2) was considerably higher than the mean for controls (36.7%; SD = 24.5) and this difference was significant in a Wilcoxon test comparing consistency pairwise for each test across the two subject groups ($Z = 2.52$, $P = .012$). This type of superior performance is taken as the behavioural 'gold standard' hallmark of synaesthesia (e.g., Asher et al., 2009; Beeli, Esslen & Jäncke, 2005; Hubbard, 2007; Rich et al., 2005; Rouw and Scholte, 2007; Ward et al., 2006; Weiss & Fink, 2009; see especially Kay, Carmichael, Ruffell & Simner, 2015, for a discussion of consistency in sequence-personality synaesthesia).

Table 2. Mean percent consistency in synaesthetes versus controls for each of 8 different variants of sequence-personality synaesthesia, with standard deviations shown in parentheses.

Type of sequence-personality synaesthesia	Synaesthetes %	Controls %
letter-gender	79.2 (14.2)	63.1 (11.2)
letter-personality	65.4 (22.8)	14.4 (8.9)
number-gender	90.0 (8.2)	52.5 (19.4)
number-personality	61.0 (30.3)	12.0 (9.5)
day-gender	81.6 (19.7)	55.7 (25.6)
day-personality	64.3 (42.5)	55.7 (25.6)
month-gender	84.4 (16.3)	15.7 (19.6)
month-personality	64.6 (27.4)	14.2 (11.8)

3.2 Imaging results. TBSS showed significant between-group differences in five areas of the brain with reduced FA in synaesthetes relative to controls (Table 2 and figure 1). These regions were the genu, body and left side of the corpus callosum, the left superior corona radiata, and pre-/postcentral gyrus/dorsal corticospinal tract. No areas of the brain showed increased FA in the synaesthete group. Table

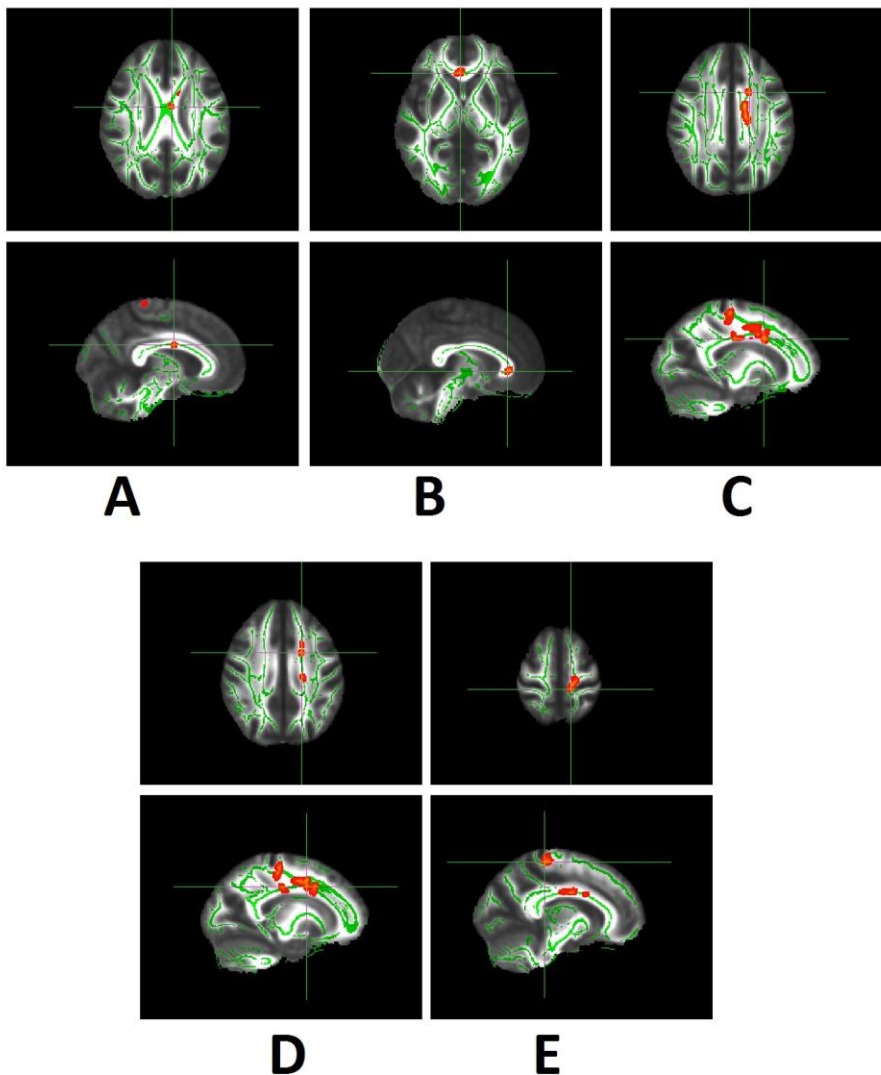
2 shows the cluster size and MNI coordinates of these results in more detail, and images of the five significant regions are each indicated by cross-hairs in Figure 1.

Table 3. Areas of the brain showing significantly reduced FA in sequence-personality synaesthetes compared to matched controls. The anatomical location, cluster size, and MNI coordinate of most significant voxel are shown.

Anatomical location	size (voxels)	max voxel MNI coordinate (mm)		
		x	y	z
body of corpus callosum	8	-5	-5	26
genu of corpus callosum	29	3	28	1
corpus callosum (left)	63	-17	9	32
Left superior corona radiata	85	-18	3	38
Left precentral/postcentral gyrus / dorsal corticospinal tract	334	-11	-32	60

Figure 1. Areas of the brain showing significantly reduced FA in sequence-personality synaesthetes compared to matched controls. Five clusters in (A) body of corpus callosum (B) genu of corpus

callosum (C) corpus callosum (left) (D) Left superior corona radiata, and (E) left precentral/postcentral gyrus / dorsal corticospinal tract.



4. DISCUSSION

In this study we compared white matter microstructure in the brains of people with OLP/ sequence-personality synaesthesia with a group of non-synaesthetic controls. We identified five clusters of white matter that had reduced FA in sequence-personality synaesthetes: left pre/postcentral gyrus/dorsal corticospinal tract; left superior corona radiata; corpus callosum (left); genu of corpus callosum; and body of corpus callosum. The current findings support existing studies showing that white matter microstructure is altered in those who experience synaesthesia (e.g., Rouw & Scholte, 2007), and here

we demonstrate that this is true whether the merged behavioural modalities of the synaesthesia are sensory (as tested previously) or cogno-social (as tested here).

Three of the areas identified in this study are located in the corpus callosum. This is the largest white matter fibre tract in the human brain which joins the left and right hemispheres, thus providing bilateral integration of neural functions (see for example, Mooshagian, 2008). Due to its central role in connecting cortical regions in both brain hemispheres, the corpus callosum influences a broad range of essential processes, from relatively low level functions such as motor skills (van Kooij et al., 2008) and bimanual coordination (Gooijers & Swinnen, 2014) to higher level functions such as those involved in language (Dougherty et al., 2007) and metrics of intelligence (Hutchinson et al., 2009, Yu et al., 2008). Perhaps importantly for this study, the corpus callosum also plays a role in social cognition. Individuals with agenesis -- i.e., complete or partial absence -- of the corpus callosum (AgCC), often show deficits in a range of social cognitive tasks. For example, Bridgman, Brown, Spezio, Leonard, Adolphs, and Paul (2014) found that AgCC patients performed poorly when asked to name the emotion displayed in a series of faces. Similarly, AgCC patients perform worse than control subjects in understanding emotional-prosodic cues (Paul, Van Lancker-Sidtis, Schieffer, Dietrich & Brown, 2003), in understanding and discussing socially complex scenes (Paul, Schieffer & Brown, 2004), and understanding humour (Brown, Paul, Symington & Dietrich, 2005) -- despite having equivalent IQs to control participants. Deficits in social cognition are also found in patients with degraded, even if not absent, corpus callosi. In such cases, the white matter microstructure of the corpus callosum has been directly associated with performance on a range of social cognition tasks. For example, Downey et al. (2015) report a correlation between reduced FA in this region and the capacity to recognise emotions portrayed in a series of short videos, based on patients whose degraded corpus callosi was tied to frontotemporal dementia. Furthermore, Miyata et al. (2010) report that patients with degraded corpus callosi (this time tied to schizophrenia) performed worse than controls in recognising emotions portrayed in verbal

and visual stimuli in social scenarios. In summary there have been number of studies linking the integrity of the corpus callosum with a range of socio-emotional tasks, and this may be particularly relevant given our participants with reduced FA in this region show unusual socio-emotional responses to stimuli.

Aside from the corpus callosum, we also found reduced FA in the superior corona radiata and the left corticospinal tract both of which may be linked to the inducer of synaesthesia. Both regions play a role in numerical cognition, and we report that 11 out of 12 synaesthetes had personifications triggered by numbers. Current evidence suggests both the superior corona radiata and the left corticospinal tract are part of the distributed frontoparietal network of interconnected brain areas that guides many aspects of numerical cognition, such as mental arithmetic and judgements of numerical magnitude (Matejko and Ansari, 2015). For example, FA values in the left superior corona radiata and the left corticospinal tract positively correlated with performance on a standard mathematics test administered to school children in the USA (Matejko, Price, Mazzocco, & Ansari, 2013). Furthermore, white matter integrity of the left superior corona radiata was associated with solving basic arithmetic problems in a study by van Eimeren et al. (2010). Because these regions are linked to numerical cognition and because the synaesthetic participants in this study experience a form of synaesthesia that is triggered by numbers, lower FA these two regions might therefore link to the fact that these brain areas are particularly associated with this form of synaesthesia. Also relevant to the current study, Cantlon et al. (2011) found that performance on number judgement tasks was related to structural differences in the white matter of the corpus callosum -- another key region implicated in our data.

Both the left superior corona radiata, and the body of the corpus callosum, were also among 28 regions found by Whittaker et al. (2014) to have reduced FA in synaesthetes -- this time in grapheme-colour

synaesthetes. Their study showed that these two regions were implicated, particularly, in mental imagery differences between synaesthetes and controls. Correlations of another white matter microstructure measure (λ_{23} , perpendicular diffusivity) were stronger in synaesthetes than controls, when comparing the integrity in each region against an imagery score (Vividness of Visual Imagery; VVI, Marks, 1973). It may be that differences in imagery are common across a range of synaesthesia (and indeed this certainly seems to be the case in behavioural terms; see Barnett & Newell, 2008; Simner, Mayo & Spiller, 2009; Rizza & Price, 2012; Havlik, Carmichael, & Simner, 2015). If imagery differences are at the root of the current findings in the corona radiata and body of the corpus callosum, these would join a third region -- the cuneus -- also implicated in imagery differences in sequence-personality synaesthesia in an fMRI study by Amin and colleagues (Amin et al., 2011).

However, the largest area of the brain showing reduced FA in our sequence-personality synaesthetes was the left precentral/postcentral gyrus. This region is primarily associated with sensory-motor functions, but this region of the precentral gyrus has also been strongly implicated in social processing, particularly within the population of people with autism spectrum conditions (ASC). Nebel, Eloyan, Barber and Mostofsky (2014) found that functional connectivity in this region is predictive not only of the odds of having ASC in their patient population, but also of their scores on the *Social Responsiveness Scale* (SRS; Constantino et al., 2003). Scores on this scale can be important in the clinical identification of people with autism, but they are also continuously distributed in the general population. The SRS quantifies an individual's motivation to engage in social interactions, and their ability to recognize emotional and interpersonal signals from others. The current finding of significant differences in this region of the precentral gyrus in sequence-personality synaesthetes might be interpreted as a link

between function and structure in our synaesthetes, since they show a particular tendency to project social, emotional and interpersonal signals onto unusual stimuli.

Our key finding in this area of pre/post-central/dorsal corticospinal tract is noteworthy also, because it, too, features in another DTI study on synaesthesia. Rouw and Scholte (2007) found significant FA differences in this area, and their peak MNI coordinates (-20,-25, 55) fall within the significant region reported here. There are two reasons why studies looking at ostensibly different types of synaesthetes might show similar regions implicated (assuming these similarities are not caused by methodological limitations; see Hupé & Dojat, 2015, for discussion). The first reason for overlaps across different forms of synaesthesia is that some regions may be tied to the synaesthetic experience irrespective of the particular variant. Shared regions could therefore be important because they capture what Rouw et al. (2011) describe as ‘a general synaesthetic constitution’ (p. 235); i.e., characteristics that are part of synaesthesia as a trait, versus any one type of synaesthesia in particular. We noted above that the findings of reduced FA in left superior corona radiata and the body of the corpus callosum have also been found among 28 regions implicated in grapheme-colour synaesthesia and attributed to imagery differences (Whittaker et al., 2014 testing grapheme-colour synaesthetes). It may therefore be that such regions tied to imagery are part of an overarching ‘synaesthesia architecture’ shared across multiple manifestations of the condition (as suggested too by behavioural data; e.g., Barnett & Newell, 2008; Havlik et al., 2015).

Alternatively, the fact that different studies find similar regions when ostensibly testing different types of synaesthesia could suggest some overlap in phenotype -- even though this may not be apparent when reading the study reports. Important here is that different types of synaesthesia -- including sequence-personality and grapheme-colour -- tend to co-occur to some extent within individuals (e.g., Simner et al., 2006; Simner & Holenstien, 2007). It is therefore likely that at least some of the

grapheme-colour synaesthetes tested in previous studies may also have had sequence-personality synaesthesia, and vice versa here, an issue that has been largely overlooked in the literature. We assume, however, that study-findings will tend to reflect the type of synaesthesia dominant in the sample (here, sequence-personality synaesthesia) but suggest one should be open to the idea that overlaps across studies might be due to the more prosaic possibility that synaesthetes are difficult to classify along just one dimension. Our own sequence-personality synaesthetes reported the following additional synesthetic variants in small numbers (n=1-3): shapes triggered by sounds and tastes; colour triggered by music, touch, days, months, voices, and shapes; spatial arrays triggered by sequences. Over 50% reported some degree of grapheme-colour synaesthesia (58.3%; n=7) although more than 40% of our sample had no grapheme-colour synaesthesia at all. In the current study we nonetheless have evidence to some extent of an architecture not found elsewhere in other forms of synaesthesia. Although the pre/post-central gyrus showed differences both here and in Rouw and Scholte (2007), their grapheme-synaesthetes showed significantly increased FA while our sequence-personality synaesthetes showed significantly reduced FA. Finding the same region implicated differently in two different types of synaesthesia suggests this area may be particularly vulnerable to disruption in people who develop synaesthesia. If so, lowered FA may result in cogno-social variants of synaesthesia as suggested here, while increased FA is apparently tied to developing other forms such as grapheme-colour synaesthesia. The social-processing function of this region is evident in the concurrent of sequence-personality synaesthesia, although not in grapheme-colour synaesthesia; in the latter it might therefore play a more epiphenomenal role, perhaps altering grapheme-colour synaesthetes' scores on social responsiveness, a possibility we are now exploring in our lab.

There are several limitations to this study which could be explored in future studies. Further testing might explicitly measure social responsiveness of each participant group given that some of the brain regions showing lower FA in synaesthetes have been implicated in this characteristic. We anticipate

that social responsiveness would indeed differ across groups given that this is perhaps *a priori* tied to what it means to be an OLP synaesthete. However, better understanding of behavioural measures might give insights into how this plays a role in altered white matter infrastructure in these brain areas. Similarly, mental imagery was not assessed in the participants of this study, which may also influence synaesthesia, and in turn affect connectivity in the brain areas reported here. We also acknowledge that due to the rarity of this form of synaesthesia, our sample of synaesthetes was relatively small for a study of this type and accordingly, our results should be viewed with appropriate caution. In addition to the variables discussed above (e.g., mental imagery), the possibility that the white matter differences between groups may originate from factors that are as yet unidentified cannot be excluded.

Finally, we discuss why it might be that our study found reduced FA (a proxy for reduced connectivity) in OLP synesthesia, even though this is a syndrome characterised by what could be argued are *increased or additional* abilities (in that synesthetes experience *additional* sensations compared to the average person). It is important to note that our result is in fact compatible with a number of other studies -- in both synaesthesia and elsewhere -- all showing reduced FA in tandem with 'additional' behavioural experiences. These include, for example, studies associating posterior tract reductions in FA with visual and other hallucinations (Ashtari et al., 2007; Fujiwara et al., 2007). In synaesthesia research, too, although DTI studies have tended to emphasise their findings of higher FA, many have also found reduced FA, as here. Specifically, just three studies found only higher FA values in synaesthete (Rouw & Scholte, 2007; O'Hanlon et al., 2013; Zamm et al., 2013) while a further three found lower FA as well or exclusively (Melero et al., 2013; Hänggi et al., 2008; and Whitaker et al., 2014 respectively). Yet other researchers may have been in a position to find reduced FA but stated *a priori* they would not to explore this direction within their results (Jäncke et al., 2009). Moreover, at least one functional study of synesthetes found a *deactivation* of certain areas in response to synesthesia-

inducing stimuli (Paulesu et al., 1995). In other words, previous synesthesia studies have found what we might consider, more properly, a pattern of *altered* FA (or functionality) rather than exclusively increased FA, and we wish to draw attention to this here. We therefore conclude that synesthesia is unlikely to be caused by a simple increase in the number or functionality of connections in the brain (see Mitchell, 2013, for a similar argument) but rather, that the literature today is instead supportive of a model in which the synaesthete brain has *altered* structure, with pockets of both increased and decreased FA from one form of synaesthesia to another, and even with a single variant.

In summary, we have demonstrated that sequence-personality synaesthetes show altered white matter microstructure in five brain regions of reduced FA. These regions play a role in social and numerical cognition, which may reflect the two crossed modalities of this cogno-social form of synaesthesia. The historical and contemporary literature has tended to describe synaesthesia as a crossing of sensory functions, often as a specific definitional criterion (see Simner, 2012 for discussion). Implicit in such definitions is the assumption that the neural underpinnings of synaesthesia in the brain could only ever give rise to sensory manifestations of the condition. We have shown here that the phenomenology of our subjects (i.e., conscious, life-long, automatic experiences of unusual crossmodal mappings) are not only typical of synaesthesia, but they also rest on comparable neural foundations involving differences in white matter coherence in the brain. Some of the patterns reported here have previously been reported in DTI studies of synaesthesia and some are novel. This suggests that different subtypes of synaesthesia can differ in architecture, but might also share overlapping neural mechanisms to some extent. We call for greater attention on definitions of synaesthesia, since our

data indicate that atypical neural connectivity has a broader scope in synaesthesia phenomenology than previously known.

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Acknowledgements. Author JS was supported by the European Research Council under the European Union's Seventh Framework Programme (FP/2007-2013) / ERC Grant Agreement n. [617678]. AMM and SML were kindly supported by the Dr Mortimer and Dame Theresa Sackler Foundations. We are grateful to Andrea Rabinowitz and Mohammad Lone for their help collecting behavioural control data, and to the DTI team at SBIRCS, Western General Hospital, Edinburgh. We are grateful, too, to T.W.J. Moorhead for his help in an earlier approach to our analyses. Correspondence and requests for materials should be addressed to JS (e-mail: j.simner@sussex.ac.uk).