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Synesthesia & Autistic Features in a Large Family:
evidence for spatial imagery as a common factor

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Abstract

Background. Autism and synesthesia are neurodevelopmental conditions associated with variants of perceptual processing. They also share some genetic variants and include a large magnitude of intra-categorical variation: 60 types for synesthesia, as well as a *spectrum* for autism. In order to investigate the relationship between these two phenomena, we investigated the family of FC, an autistic individual who also possess savant abilities and synesthesia manifestations.

Method. Autistic symptoms were assessed for the entire sample of participants entering the study (39 individuals) using the SRS. Participants above threshold were evaluated with standardized diagnostic tools. Synesthesia was explored in the entire participating sample using a self-reported questionnaire. Consistency tests were used for participants who reported synesthetic manifestations.

Results. In addition to FC, four individuals with ASD were detected. Fifteen participants self-reported synesthesia (15 sequence-space, 4 sound-shape, 4 lexical-color), among which nine sequence-space synesthetes satisfied the consistency criteria. Two participants possess both autism and synesthesia.

Conclusion. This family illustrates the co-segregation of autism and synesthesia. This co-segregation is in favour of a partially overlapping genetic predisposition for both conditions, but also authorizes a large variety of manifestations in both conditions. The high prevalence of sequence-space synesthesia in this family strengthens the previous assumption that this form of synesthesia may be linked to autism. We discuss the potential role of spatial imagery in the development of this form of synesthesia and savant abilities.

Keywords: autism, synesthesia, spatial imagery, inheritance, genetics

1. Introduction

Autism and synesthesia are two neuro-developmental conditions that were seen as unrelated for a long time. However, recently it has been suspected that they may share some cognitive, connectivity and genetic characteristics. In this paper, we investigate among the large family of FC, an individual with the presence of both conditions, having Autism Spectrum (AS) and possessing several savant abilities and synesthesia manifestations.

AS is a frequent neuro-developmental disorder that encompasses social and communication atypicalities, associated with restricted interests and repetitive behavior. The causes of AS are unknown, but genetics factors are largely involved, leading to a micro and macro structural brain alteration (Bourgeron, 2015). While the majority of the AS phenotype is associated to a large number of common genetic variants with small effects (Girirajan & Eichler, 2010), 10 to 20% of people with autism also present rare identified syndromes with large effects, mostly deleterious and lowering IQ. The prevalence of individuals in the AS, as currently defined in DSM and operationalized in standardized diagnostic instruments, is estimated at 1 to 68 individuals (Christensen et al., 2016). While prototypical forms may benefit from a categorical and reliable diagnosis (de Marchena & Miller, 2017), less distinct, degraded manifestation of the phenotype or autistic features are largely spread in the general population. Although mechanisms of genetic transmission are unknown, this risk of belonging to the AS is increased 22 times for siblings of non-syndromic autistic children (Lauritsen, Pedersen, & Mortensen, 2005). However, the estimation of autistic genetic inheritance is largely dependent of the stringency of the phenotype under study (categorical diagnosis, or features). AS individuals also present atypical perceptual processing and perception-based behaviors, which is now included in autism diagnostic criteria. Following the enhanced perceptual functioning model, their perception plays a superior role in their cognitive processes, is more autonomous from top-down influences and perform better than in typical individuals (Mottron et al., 2013; Mottron, Dawson, Soulieres, Hubert, & Burack, 2006).

Synesthesia is a subjective phenomenon where the perception of one particular stimulus automatically elicits an idiosyncratic perception in the same or different sensory modality. The most common are the *sequence-space* synesthesia, for instance when months are associated to specific spatial localizations, *grapheme-color* synesthesia where, for instance, letters are

associated to specific colors, and *colored-hearing* synesthesia, where sounds are associated to specific colors (Ward, 2013). Since synesthesia is a subjective phenomenon, there has been search for objective testable criteria. Consistency, idiosyncrasy and vividness of association are now recognized as the gold standard of synesthesia. Described at first as perceptual phenomenon, it is now accepted that higher order cognitive processes are involved, such as language in grapheme-color synesthesia (Simner, 2012). Various forms of synesthesia have been depicted besides the most typical form, which is grapheme-color or sound-color synesthesia (at least 60; Day, 2005). Sequence-space synesthesia is estimated to occur in 8–12% of the general population (Chun & Hupé, 2013; Ward et al., 2018). Lexical color forms of synesthesia are estimated to occur in 4.1% of the population (Chun & Hupé, 2013). As autism, synesthesia can be described as a spectrum with some ‘weak’ forms, which are common, and some less common cases possessing strong, reliable, complex, or multiple forms of synesthesia. The question of a continuum between multimodal association and synesthesia, the latter falling at the extreme end of continuum, is an ongoing debate in the field (Deroy & Spence, 2016) .

There is a strong genetic component in the occurrence of synesthesia: the prevalence of synesthesia is greater than 40% amongst the first or second order degree relatives of synesthetes (Baron-Cohen, Burt, Smith-Laittan, Harrison, & Bolton, 1996; Ward & Simner, 2005). Different type of synesthesia can be observed within the same family (Barnett et al., 2008). No identified gene is causative in synesthesia, rather multiple genes at multiple loci represent predisposing factors (Asher et al., 2009; Tilot et al., 2018; Tomson et al., 2011). Synesthesia is thought to be associated to hardwired neurological atypicalities (Hupé & Dojat, 2015), but unravelling common neurological mechanisms to multiple forms of synesthesia has been a challenge, due to the relatively small size of the groups presenting the same type. However, for auditory visual synesthesia several studies showed an enhanced connectivity in cross-modal areas (Brauchli, Elmer, Rogenmoser, Burkhard, & Jäncke, 2018; Goller, Otten, & Ward, 2009; Neufeld et al., 2012).

The higher prevalence of grapheme color synesthesia in AS has been shown recently (Neufeld et al., 2013). In comparison, similarities between perceptual alterations encompassed under the enhanced perceptual functioning cognitive theory in AS and those evident in synesthesia have been empirically demonstrated. For instance, individuals with synesthesia show a score of behavioral attention to details, measured with the autism quotient (AQ; Baron-Cohen,

Wheelwright, Skinner, Martin, & Clubley, 2001) similar to individual with AS (Ward, Brown, Sherwood, & Simner, 2017; Ward, Hoadley, et al., 2017). Synesthete and AS people also shared superior sensory sensitivity in comparison to typical individuals (Ward, Hoadley, et al., 2017). At the genetic level, and beyond the uncontested familial aggregation of the two conditions taken separately, a significant connection between genes previously shown to be associated with AS and those associated with synesthesia has been reported (Asher et al., 2009).

Case studies of AS individuals with savant abilities and synesthesia have been reported occasionally (see for instance Bor, Billington, & Baron-Cohen, 2007; Bouvet et al., 2014). It has been hypothesized that the co-occurrence of the two neurodevelopmental variants is enough to produce savant abilities (Hughes, Simner, Baron-Cohen, Treffert, & Ward, 2017). In the same vein, we have proposed that an overarching neurocognitive mechanism, *veridical mapping*, might explain synesthesia, absolute pitch, and savant abilities in AS (Mottron et al., 2013). Due to a hyper microstructural perceptual plasticity found in AS (see Mottron, Belleville, Rouleau, & Collignon, 2014 for a review) the neural coding for the cross-modal associations between homologous elements belonging to large series of perceptual representations (e.g., printed character / sound for hyperlexia, letters / colors for synesthesia) would stabilize along development. The persistence of these physical connections would be responsible for the cross-modal perceptual activation (subjectively perceived in the case of synesthesia or absolute pitch), as well as for the apparently ‘‘automatic’’ cross-domain rehearsal of cognitive material, in absolute pitch and hyperlexia.

In this paper, we present the large family of FC, an AS individual who possesses several savant abilities, synesthesia, and absolute pitch. In-depth phenotypic characterisation of the autistic and synesthetic manifestations may highlight how a genetic constraint applies to phenotypic manifestations, as well as provides a factual example of which autistic and synesthetic manifestations are aggregated in the same family.

2. Method

2.1. Population

The family is two generations composed of 11 brothers and sisters and their children, for a total of 46 members. One member, FC, is autistic and possesses multiple savant abilities (absolute pitch, mental calculation, calendar calculation) as well as synesthesia manifestations. A

detailed case study has been carried out on his savant abilities and their relation with synesthesia (Bouvet et al., 2014). 39/46 members of his family (23 males, 16 females, 11 to 64 years old) agreed to participate to the study (see Figure 1).

2.2. Autism evaluation

Autistic symptoms were screened with the Social Responsiveness Scale (SRS, Constantino & Gruber, 2005) in the entire sample of participants. When t score was above the 50 percentile and clinical signs were observed, AS was investigated with direct standardized observation by trained specialists using ADOS module 4 (Hus & Lord, 2014) and ADI-R (Lord, Rutter, & Le Couteur, 1994).

2.3. Synesthesia evaluation

All members of the family were screened for synesthesia with a self-report questionnaire including a short description of synesthesia, followed by closed questions specific to each type of synesthesia. For instance, for grapheme-color synesthesia: do you associate colors to numbers or letters; for sequence-space synesthesia: do you see number in a specific position; for color-sound synesthesia: do sounds evoke specific colors. Fifteen individuals reported the possession of synesthesia. Different types of synesthesia were identified: sequence-space synesthesia (12), sound-shape synesthesia (6), lexical-color synesthesia for weekdays (4), sound-color synesthesia (1). Some individuals reported several forms of synesthesia. Experimental tests were developed in order to evaluate the consistency of sequence-space and lexical-color. Sound-shape consistency was not evaluated, due to the synesthetes' difficulties to represent graphically their perception of dynamic shapes. However, we report the description of their perception in Table 1.

2.3.1. Sequence-space synesthesia

To evaluate the consistency of the synesthesia, participants were asked to complete a computerized test inspired by previous studies on sequence-space synesthesia (Brang, Teuscher, Ramachandran, & Coulson, 2010; Rothen, Jünemann, Meador, Burckhardt, & Ward, 2016). Four different tests evaluated their representation of days ($n=7$), months ($n = 12$), numbers (digits 1-10), and tens number (10 to 100). The experiment was run with PsychoPy software (Peirce,

2007). In each test, participants were asked to project their mental representation on the computer screen and to click at the exact localization of each item. On each trial, the instruction “Place X” (Monday, January 1 or 10) was presented at the top center of the screen until the participant moved it for their response. The localization of each item was asked six times, and items were randomized. X/Y screen coordinates were recorded on each trial. From the three X/Y coordinates of the last three trials, a triangle was built for each item, which correspond to its spatial location. The area of the triangle is used as a quantifying index of the consistency of the synesthetic representation (Rothen et al., 2016). Consistency is ascertained when this area is inferior to 0.203% of the screen (1366 *768 pixels in this study). Furthermore, consistency scores exceeding 2 standard deviations from the mean in each experiment were considered as deviant.

2.3.2. Lexical-color synesthesia for weekdays

To evaluate the consistency of this type of synesthesia, names of week days were presented to participants in size 40 Arial black font, in PowerPoint© software. Each day name was written in a random color. For each day, participants were asked to choose the appropriate color according to their perception using the color palette of PowerPoint. The color of each day was asked four times, and each trial used a different sequence of days and color of the day. For one participant, the day colors were only asked two times due to time constraints, thus consistency could not be assessed for this participant. For the three participants, a consistency score was computed across the four trials which reflect how far away in color space those four colors were, averaged across all weekdays. A score less than 1.49 indicates a consistency of the association typical of synesthesia as recommended (Rothen, Seth, Witzel, & Ward, 2013).

2.3.3. Sound-color synesthesia

This synesthesia was evaluated with the online version of Synesthesia Battery (<https://www.synesthete.org>; Eagleman, Kagan, Nelson, Sagaram, & Sarma, 2007), which evaluates the internal consistency of sound-color associations. In this test, sounds of 13 pitches (from C4 to C5, piano timbre) and 18 instruments are played several times, and the participant has to randomly select a color for each sound. This test evaluated the consistency of responses across trials by calculating the color variation between different trials. A score below 1.49

indicates consistency of association while a score above 2 indicates an absence of synesthesia (Eagleman et al., 2007).

In addition to consistency, idiosyncrasy of the association and its vividness were also considered for evaluation of synesthesia, as recommended by Simner (2012). A questionnaire was also proposed in order to evaluate the idiosyncrasy of their representation inspired of the Synesthesia Battery (Eagleman et al., 2007). This questionnaire explored the synesthesia furthermore (the beginning of the synesthesia, the consistency, the automaticity). There were also questions about the visualization of the sequence and a drawing of their representation for sequence space synesthesia. Participants could also add any information that they think can be related to their synesthesia.

3. Results

3.1 Autism

Besides FC who was already diagnosed autistic, four other individuals were identified as belonging to the autism spectrum. Thus, five family member possess a categorical diagnosis within the autism spectrum. The prevalence of AS in this family is 12.82% (95% Wald confidence interval: 5.6 % to 26.71 %) exceeding the prevalence of 1.4% observed in the general population (Christensen et al., 2016)

3.2. Synesthesia

Of the 15 members who reported synesthesia, one refused to continue the study. Another one reported the perception of visual-spatial representation of number (from 1 to 10, as on dominoes), which cannot be considered synesthesia. Therefore, only 13 were tested. We report synesthesia self-description as well as observations and results of the consistency test in Table 1. Of the 12 individuals who reported sequence-space synesthesia, 9 satisfied both the criteria of consistency (consistency score below cut-off and below two standard deviations of the mean) and the vivacity of the description. The three individuals tested for lexical-color synesthesia satisfied the criteria of consistency, but for one participant the associations were not idiosyncratic (i.e., colors were learnt at school and have a signification, see Table 1). Testing of sound-color synesthesia revealed that only one sound was associated to a specific color for the individual who

reported it. Taken together, results indicated that among the 13 individuals who reported synesthesia and were evaluated for this, 9 verified the main standard of synesthesia, which is the stability of their association and/or the idiosyncrasy of their representation (see Table 1). All 9 synesthetes possess sequence-space synesthesia. They represented 23.09 % (95% Wald confidence interval: 12.65% to 38.34%) of the 39 family members willing to participate to this study, exceeding the prevalence of 8.1-12.8% observed in the general population (Ward et al., 2018).

3.3. Report of subjective manifestations

Four participants (including one who did not report sequence-space synesthesia) reported vivid imagery for geographic places. They reported, when hearing the name of a city, the visualization of the localization on a map directly, as well as pictures of the localization. Some of them used the analogy of google maps© to describe this ability. One member experienced ticker tape manifestation (i.e., he automatically visualized spoken words), vivid geographic mental imagery, and specific association between places and words or actions. Furthermore, he perceives a specific place when performing a certain action. For example, when doing his hair in the morning, he sees a specific place of the yard of his former high school. For him, many words or subjects of conversation are “stored” in a specific known place (see details in Table 1).

3.4 Autism / synesthesia relations

Besides FC, who possesses typical autism and synesthesia like manifestation, two individuals were identified as possessing synesthesia and AS. It is worth noting that these two individuals are brothers and they reported two forms of synesthesia (sequence – space and sound – shape). Both of them reported vivid imagery for geographic places and one also reported ticker tape manifestation and specific association between places and words or actions.

4. Discussion

This is the first study of autistic and synesthetic manifestations in a large family (46 members) related to the first and second degree, and to an individual presenting both conditions and savant abilities. We observed a **higher** presence of AS and sequence space synesthesia. The

higher prevalence of AS manifestations along with a specific form of synesthesia, sequence-space synesthesia in this family, highly suggests partially overlapping genetic and cognitive mechanisms in these two conditions.

What is the connection between autism and synesthesia at the cognitive level? Previous studies have shown shared neurocognitive atypicalities between sequence-space synesthesia and AS. Sequence-space synesthetes are those presenting a superior attention to detail (as measured by AQ) compared to controls (Mealor, Simner, Rothen, Carmichael, & Ward, 2016; Ward, Hoadley, et al., 2017). Importantly, Ward et al (2018) demonstrated that sequence -space synesthetes show several indications of enhanced visual perception compared to non-synesthetes (superior mental imagery, stronger spatial interference, and detection of low visibility stimuli). Therefore, one of the shared cognitive mechanism between autism and synesthesia may be spatial mental imagery. Mental imagery can be divided into a spatial component, specifying the visuo-spatial relationships between features and allowing mental manipulation of spatial material; and a visual component, the verbal and conceptual labels enabling a vivid and concrete representation of the object (Kosslyn et al. 2006). Whereas superior imagery has been described in different type of synesthesia (Barnett & Newell, 2008; Chun & Hupé, 2016; Spiller, Jonas, Simner, & Jansari, 2015) sequence-space synesthetes possess higher spatial imagery than lexical-color synesthetes (Jonas & Price, 2014; Mealor et al., 2016). In autism spectrum, superior abilities in mental rotation task, a proxy of mental imagery has been reported (Falter, Plaisted, & Davis, 2008; Hamilton, Brindley, & Frith, 2009; Pearson, Marsh, Ropar, & Hamilton, 2015; Soulières, Zeffiro, Girard, & Mottron, 2011). Consistent with this interpretation some individuals in our sample reported abilities related to spatial imagery: zooming in and out on their sequence-space representation for 3 sequence-space synesthetes; immediate visualization of places when reading maps for four individuals; sound-shape synesthesia. (i.e., perception of a dynamic shape with no specific color when hearing sounds) for four individuals. Moreover, two individuals show AS manifestations, sequence-space synesthesia and vivid spatial imagery (see Table 1 and Figure 1 for details).

Not only may vivid spatial imagery be shared between autism and synesthesia, but their combination may contribute to the development of savant abilities. Synesthesia is higher among AS individuals who possess savant abilities (Hughes et al., 2017). More specifically, Simner et al. (2009) suggested that sequence-space synesthetes are predisposed to develop savant abilities. For

example, one individual, AC, reported vivid mental imagery of geographic places but also for words (i.e., visualization of words when hearing them) and specific actions in addition to sequence-space & sound-shape synesthesia. AC was also identified as belonging to the AS. A contribution of mental imagery and especially, spatial imagery in combination with synesthesia to the development of savant abilities is congruent with the veridical mapping model (Mottron et al., 2013). This framework hypothesizes a common neural encoding of elements sharing a similar location in an abstract, but spatialized structure in different perceptual modalities. Thus, this ability contribute to the development of special abilities in the context of autism, particularly hyperlexia, absolute pitch, and calendrical calculation.

Besides the link between AS and synesthesia, this study is informative on how different types of synesthesia can occur in a single family, therefore plausibly indicating sharing a common genetic trait. Indeed, we can identify in this family two familial clusters of forms of synesthesia, with different characteristics. The first cluster is composed of one father (MaC) and two of his children (DC, CC) who possess sequence space synesthesia and lexical-color synesthesia for weekdays. The second cluster is composed of one father (MatC) and his two children (AC & GC), who are the only ones among the sequence-space synesthetes to have reported the ability to manipulate their perception. All three also possess sound shape synesthesia and a vivid geographic imagery. The family under study, is therefore consistent with Barnett et al. (2008) suggestion that all forms of synesthesia share a common underlying genetic mechanism. However, it suggests that different mechanisms might be observed within the same family that result in specific subtypes of synesthesia.

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Figure 1. Family pedigree. The proband is marked with arrow. Circle indicate female and square indicate male. In grey individuals who participated to the study, in green individuals who reported synesthesia, in light blue individuals with confirmed synesthesia, in dark blue individuals with autism.

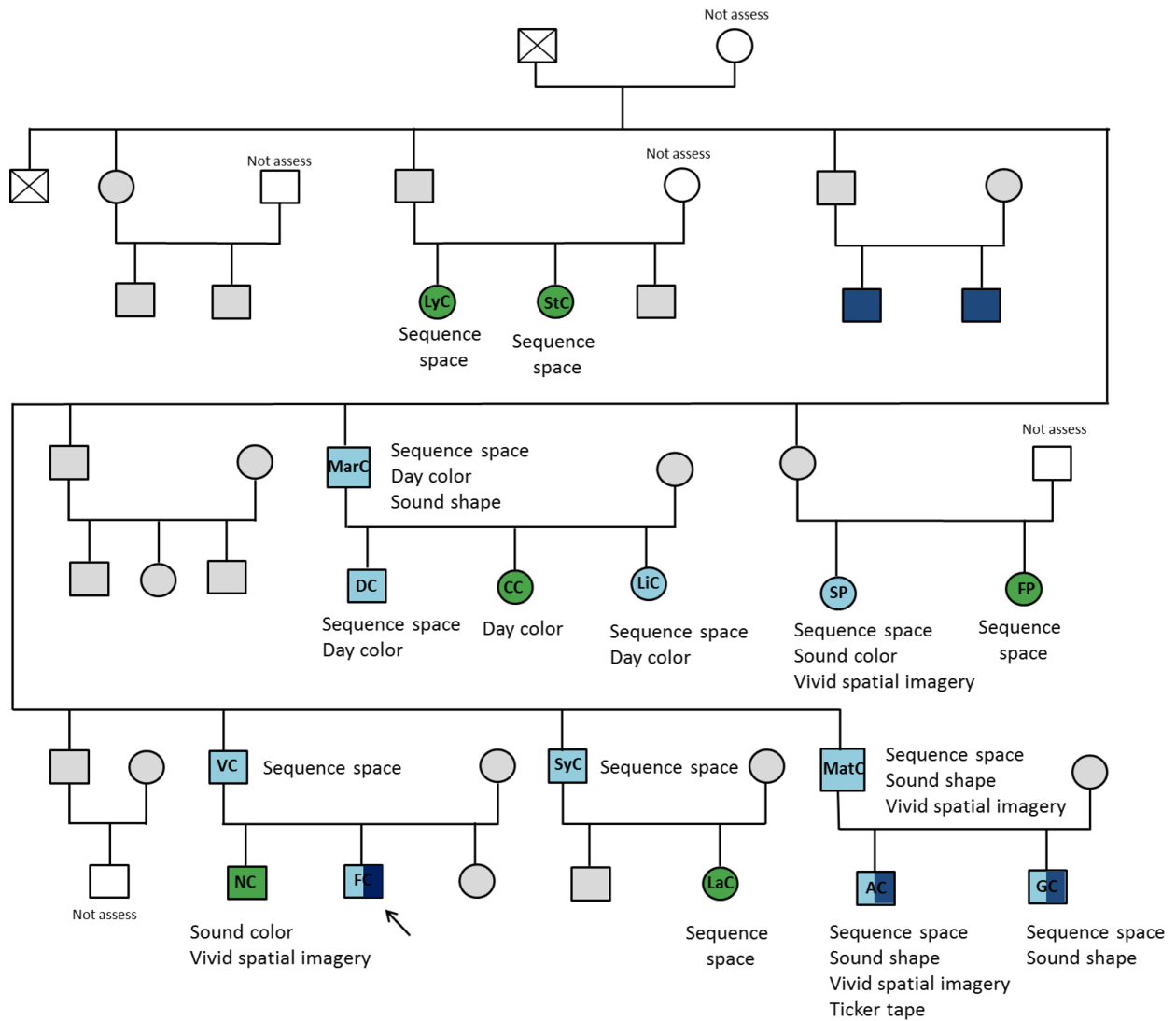


Table 1. Summary of synesthesia and AS observed among the family members

Participants (gender, age)	Type of synesthesia reported	Consistency of the synesthesia	Description of sequence space synesthesia	Description of sound-shape synesthesia	Description of other form of synesthesia or other subjective experiences	Decision regarding the possession of synesthesia	Possession of AS
AC (M, 25)	Sequence-space Sound shape	yes	Days : rectangle shape Months : circle shape Numbers : curved line on which he can zoom in and out	Perception of a dynamic complex shape that represents exactly and distinctly each sound. The texture of the shape distinguishes a sound between another like the strokes of a brush. Musical ambiance induces the perception of stable color. Physical pain also induces the perception of shape.	<i>Vivid geographic mental imagery</i> : when hearing the name of a city, visualization of the localization on a map directly as well as pictures of the localization <i>Experiencing mental imagery when performing certain action</i> : associate words, objects, or daily actions to a known place. When doing his hair the morning, perception of a specific place of the yard of his former high-school. Many words or subjects of conversation are “stored” a specific known place <i>Ticker tape experience</i> : see mentally spoken words	yes	yes
CC (F, 14)	Lexical color	no			Lexical – color Perception of color for 5 letters and 5 weekdays. Certain days have colors because they are associated to a certain activity (e.g., monday is black because it is the beginning of the week, sunday is white because it is a relaxing day). Certain day-colors associations have been learnt at school.	no	no

DC (M, 17)	Sequence-space Lexical - color	yes	Days : diagonal Months : two diagonals Numbers : curved line		yes	no
FC (M, 26)	Ordinal linguistic synesthesia	See Bouvet et al. (2014)			yes	yes
FP (F, 33)	Sequence - space	Not evaluated	Visualize a calendar when think to a specific date		no	no
GC (M, 20)	Sequence-space Sound-shape	yes	Visualization of kind of planning where days are grey when something is planned. He can zoom in and out from this planning.	Perception of dynamic colorless shapes. Each sound has its own shape that looks like to the spectrogram of the sound. When hearing complex sounds, perception of different sinewaves.	yes	yes
LaC (F, 21)	Sequence-space	For day only	Days : column Months: circle. During the test session, spatial representation of days has switched into a line. Visualization of days and months as learnt at school		no	no
LiC (F, 11)	Sequence-space Lexical color	yes	Days : circle Months : circle Numbers : curved line		yes	no
LyC (F, 39)	Sequence - space	Not evaluated	Perception of visuo spatial representation of numbers from 1 to 10		no	no
MarC (M, 57)	Sequence-space Lexical - color Sound-	Yes (not evaluated for day-color)	Days : line Months : half circle Numbers : curved line	Perception of shapes moving toward him when listening to music. High pitched sound have a crystal color and low pitched sound have	yes	no

shape

a brown color

MatC (M, 47)	Sequence-space Sound-shape	yes	For days, months and numbers, visualization of a line on which he can put a cursor and zoom in and out.	Perception of dynamic forms rather rounded when listening to music. More the sound is complex and pleasant, more the form is complex	<i>Vivid geographic mental imagery:</i> when hearing the name of a city or a place, visualization of the localization on a map as well as pictures of the place, “it is like google maps”.	yes	no
NC (M, 30)	Sound color	no			Sound-color High-pitched sounds are yellow and low-pitched sound are concave. He possesses synesthesia since 20 years old. His synesthesia is elicited by specific situation (alone, relaxed). <i>Vivid geographic mental imagery:</i> when hearing the name of a city or a place, visualization of the localization on a map as well as pictures of the place	no	no
SyC (M, 49)	Sequence-space	yes	Days : line Months : curved line Numbers : curved line			yes	no
StC (F, 43)	Sequence-space	yes	Days : line Report a blurry visualization			no	no
SP (F, 34)	Sequence-space Sound-shape	yes	Days : circle Months : column in which the month of the present day is on the top Numbers : table in which numbers are arranged by line of 5	Perception of shapes when hearing environmental sounds	<i>Vivid geographic mental imagery:</i> when hearing the name of a city or a place, visualization of the localization on a map as well as pictures of the place	yes	no

**VC
(M, 50)**

Sequence-
space yes

Months : semi-circle
 Numbers : curved line
 He reports that his
 synesthesia is fading
 with time. He was unable
 to perform the
 consistency test for
 numbers

yes no