

University of Milano Bicocca

Department of Psychology

PhD program in Experimental Psychology, Linguistics and Cognitive

Neuroscience

XXX Cycle

Curriculum Mind, Brain, and Behavior

**Visual statistical and rule learning in language,
learning and communicative disorders**



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ACADEMIC YEAR 2016/2017

*A Hermann, Chiara e Valentina,
che ancora dopo 7 anni continuano ad infondermi
la passione per questo lavoro*

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ABSTRACT

One of the central issues in the study of neurodevelopmental disorders is the investigation of domain-general cognitive abilities that could underlie complex clinical phenotypes. On this vein, it has been recently proposed that impairments in domain-general implicit learning mechanisms might underlie language and communication disorders, such as specific language impairment (SLI), developmental dyslexia (DD) and autism spectrum disorders (ASD). The present thesis had the general aim to investigate the functioning of visual implicit learning in the development of SLI, DD and ASD. Specifically, we decided to focus on visual statistical (SL) and rule learning (RL) abilities. SL allows to extract the statistical relationships embedded in a sequence of elements (Saffran et al., 1996), while RL allows to extract high-order rules from a sequence of elements and to generalize these rules to novel stimuli (Marcus et al., 1999). As these mechanisms are thought to be a prerequisite for language acquisition and the development of social understanding, they could serve as possible precursors or mediators of deficits in language and social skills that defined SLI, DD and ASD.

Here, I suggest the importance of investigating whether and how different types of learning mechanisms are related to different typical and atypical outcomes in language and communication development. To this end, we used four different approaches: 1) the study of typically developing infants; 2) the study of diagnosed children; 3) the study of infants at low risk to develop language and communication disorders by virtue of having a parent with sub-threshold high traits; 4) the study of infants with a family risk to develop these disorders by virtue of having a first degree relative with a certified diagnosis. The thesis includes four empirical studies in which we used these four different approaches. The first study provides evidence that visual RL at 7 months of age predicts grammatical outcome at 2 years in typically developing (TD) infants, showing that infants' ability to extract and generalize abstract rules from a sequence of element is related to the ability to parse the structure of language. The second study demonstrates an impairment in visual RL abilities in DD children when compared with TD children, and that visual RL is overall correlated with children's grammatical skills and in their ability to read a text. In the third study, we show that visual SL abilities are impaired in infants whose parents manifest subthreshold autistic social difficulties. Finally, the last study provides evidence for a deficit in visual RL abilities in infants with a family risk to develop SLI and DD, despite intact SL abilities.

Overall, these findings suggest that an impairment in visual implicit learning abilities can underlie the development of SLI, DD and ASD, further confirming the importance of studying implicit learning mechanisms as early markers for language and communicative disorders, which in turns has strong implications for early intervention programs.

INTRODUCTION

The present research project was focused on the role of visual statistical and visual rule abilities in specific language impairment (SLI), developmental dyslexia (DD), and autism spectrum disorder (ASD), three neurodevelopmental disorders characterized by different phenotypic clinical outcomes. SLI and DD are defined as neurodevelopmental disorders characterized by a deficit in language and reading skills respectively (American Psychiatric Association, 2013). ASD is characterized by deficits in language and communications skills, in social interaction, and by restricted and stereotyped behaviours (APA, 2013). Several studies have reported a high rate of co-morbidity between these disorders (Bishop and Snowling, 2004; Tomblin, 2011) and evidence of common genetic factors (Bishop, 2010; Pennington and Bishop, 2009; Eicher and Gruen, 2015) that might give rise to an overlap in neuropsychological deficits that mediate the atypical outcome in language and communication. On this account, the declarative/procedural model proposes the hypothesis that SLI, DD and ASD might share a common implicit learning deficit (Ullman, 2004, 2016). In line with the neuroconstructivist approach to atypical development (Karmiloff-Smith, 1998), this model proposes that an impairment in general domain learning ability could underlie distinct deficits in the language domain. Indeed, both the declarative/procedural model and the neuroconstructivist model posit that neurodevelopmental disorders emerge gradually from domain general cognitive dysfunctions in continue interactions with many diverse factors, as genes, and environments. These early dysfunctions would have a cascading effect on child development, leading to complex and atypical phenotypic outcomes. These models propose that the study of basic cognitive mechanisms, such as infants' ability to learn implicitly from the environment, as well as the investigation of their functioning in early development, are critical for a full comprehension and treatments of neurodevelopmental disorders.

In line with this approach, the present thesis had the general aim to investigate the functioning of visual implicit learning mechanisms in the development of SLI, DD and ASD. As implicit learning is a broad and complex system and many mechanisms fall under its umbrella, we decided to focus on visual statistical (SL) and rule learning (RL) abilities because both SL and RL are thought to be a prerequisite for language acquisition and social learning (e.g., Lieberman, 2000). SL allows to extract the statistical relationships (i.e., transitional probabilities) embedded in a sequence of elements (Saffran, Aslin, and Newport,

1996), while RL allows to extract high-order rules from a sequence of elements and to generalize these rules to novel stimuli (Marcus, Vijayan, Bandi Rao, and Vishton, 1999). I propose that these sequence learning mechanisms could serve as possible precursors or mediators of deficits in language and social skills that defined SLI, DD and ASD.

The idea that a deficit in implicit learning mechanisms might contribute to the impairments in SLI, DD and ASD is one of the prominent question in the study of neurodevelopmental disorders (Saffran and Kirkham, 2017; Ullman, 2004, 2016). Indeed, in the last two decades, a growing number of researches has been devoted to investigate the role of sequence learning in language and communicative (dis)abilities (Arciuli, 2017; Arciuli and von Koss Torkildsen, 2012; Armstrong, Frost, and Christiansen, 2017; Ullman, 2016). However, while many researches have been focused on the relation between SL abilities and the emergence of these disorders, the study of a possible dysfunction in RL abilities has received less attention. In order to fill this gap, the majority of the studies reported in this thesis concerns the functioning of visual RL mechanism in relation to language, learning, and communicative disorders.

More specifically, the studies reported in the present thesis focus on the role of visual RL mechanism in language outcome in typically developing infants (chapter 3) and on the functioning of SL and RL in school-age children with a certified diagnosis of DD (chapter 4), and in infants at risk for ASD (chapter 5) and SLI/DD (chapter 6). As an introduction to these empirical studies, I will describe the studies that have already investigated the role of SL and RL in early typical development and in language and communicative neurodevelopmental disorders (chapter 1), and I will explain in details our research questions and general aims (chapter 2).

The empirical studies reported in this thesis have been carried out in collaboration with the IRCCS ‘Eugenio Medea’ (Bosisio Parini, Lecco) and are part of a broad project that is aimed to investigate the early markers for SLI and DD in a multi-factorial prospective, considering different cognitive abilities as rapid auditory processing (for more details see: Cantiani et al., 2016) and visual implicit learning abilities. Overall, with this thesis, we further suggest the importance of studying implicit learning mechanisms as early markers for language and communicative disorders, which in turns has strong implications for early intervention programs.

CHAPTER 1

STATISTICAL LEARNING AND RULE LEARNING IN EARLY DEVELOPMENT: THE STATE OF THE ART

In this chapter, I will report those studies that have investigated the role of SL and RL abilities in early typical development and in language and communicative neurodevelopmental disorders.

Statistical learning

Statistical learning (SL) is an implicit learning mechanism that allows to extract transitional probabilities from a continuous string of elements (Saffran et al., 1996), where transitional probabilities are defined as the conditional probability of an item Y to follow an item X (Bulgarelli, Benitez, Saffran, Byers-Heinlein, and Weiss, 2017): $\text{probability of } Y|X = \text{frequency of } XY / \text{frequency of } X$.

The first study on SL ability was carried out by Saffran et al. (1996) with the aim of identifying the cues that drive word segmentation in preverbal infants. In this seminal study, the authors exposed 8-month-old infants to a continuous speech stream for 2 minutes. The stream consisted of four three-syllable nonsense words (i.e., *bidaku padoti golabu bidaku*) repeated in random order, in which the transitional probability between syllables was 1.0 within each word and 0.33 across words. Since the stream was presented with no pauses, stress differences, or any other acoustic or prosodic cues to word boundaries. The only cue available to chunk the speech into word-like units was the statistical regularities with which syllables co-occurred. After the familiarization, infants were presented with the statistically structured familiar sequence, and with a novel sequence that did not contain statistical cues. Results showed that infants were able to discriminate between the novel and the familiar test sequences, providing evidence that they have extracted the statistical regularities during familiarization. Although, this result revealed that preverbal infants were endowed with a powerful mechanism to learn statistical structure from a flux of speech syllables, it was not clear whether infants were sensitive only to transitional probabilities or they relied also on the frequencies of co-occurrence between syllables. Indeed, the ability to extract co-occurrence frequency is a simpler type of statistical information that involves the rate with which two items (X and Y) appear consecutively in a sequence. Computing frequency of co-occurrence requires to notice what co-occurs with what, and how often this happen (Miller and Selfridge,

1950). To isolate transitional probabilities from the frequencies of co-occurrence, in a subsequent study Aslin, Saffran and Newport (1999) have equated the words and part-word in the frequency with which their syllables occurred together. In this case, only the difference in transitional probability between successive syllables, and not frequency of co-occurrence, would allow infants to parse the speech sequence. Results showed that 8-month-old infants were still able to discriminate between novel and familiar structures during the test phase, confirming that infants detected the word boundaries relying only on the statistical information provided by transitional probabilities.

Starting from these seminal studies, a growing body of research was devoted to investigate the role played by SL in language development, reporting that it is a key mechanism involved in vocabulary acquisition (e.g., Ellis, Gonzales, and Deák, 2014; Shafto, Conway, Field, and Houston, 2012) and in many other crucial aspects of language processing, such as in the extraction of prosodic patterns (e.g., Mattys, Jusczyk, Luce, and Morgan, 1999), in the discovering of phonotactic regularities (e.g., Mattys and Jusczyk, 2001), in the match between sounds and language meaning (Estes, Evans, Alibali and Saffran, 2007), and in the phonological decoding in reading ability (Arciuli and Simpson, 2012).

SL is not limited to speech stimuli, as it operates also with non-linguistic auditory stimuli (e.g., Saffran, Johnson, Aslin and Newport, 1999), visual stimuli (e.g., Fiser and Aslin, 2001, Kirkham, Slemmer, and Johnson, 2002) and tactile stimuli (e.g., Conway and Christiansen, 2005). Focusing on the visual domain, the first study that investigated visual SL abilities was carried out by Fiser and Aslin (2001). The authors habituated 9-months-old infants to visual scenes formed by several shapes grouped into spatially-organized pairs (i.e., the circle was always located above the hourglass; Figure 1.1). After habituation, infants were presented with test pairs, followed familiar and novel spatial patterns. Infants showed a preference for novel than familiar patterns, providing the first evidence that they were able to detect relationships underlying structures of the visual scene by tracking conditional probabilities, wherein the pairs were equating for frequencies of co-occurrence. This finding provided evidence that infants in the first years of life are able to extract the transitional probabilities embedded in an array of visual elements.

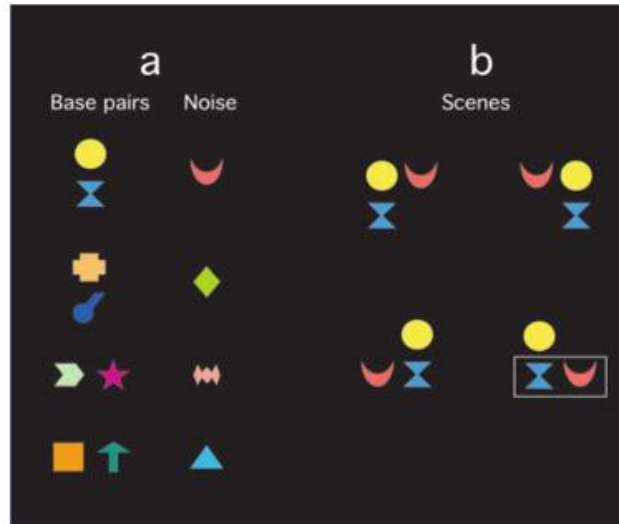


Figure 1.1: Example of visual arrays used in the study of Fiser and Aslin (2001). In the left sides (a) are represented the target (base pairs) and distractors (noise). In the right sides (b) are represented four possible scenes presented during the test phase composed by target and distractors.

Capitalizing on this evidence, Kirkham and colleagues (2002) investigated preverbal infants' ability to learn a sequential visual input. Infants at 2, 5, and 8 months of age were habituated to a visual sequence of geometrical shapes presented one at a time like in a continuous manner. The sequence was composed by 3 pairs of shapes presented in random order, hence, the predictability between shapes within each pair was 100%, whereas the predictability between shapes across pairs was 33% (see Figure 1.2).

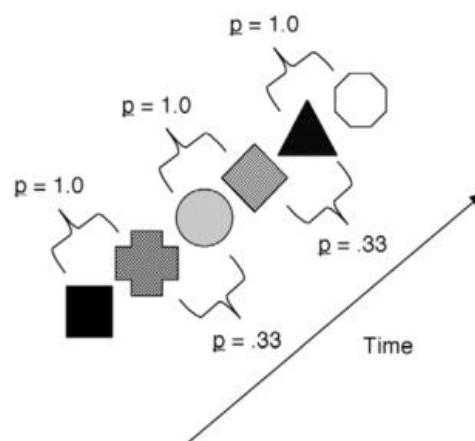


Figure 1.2: A schematic representation of the stimuli used in the study by Kirkham et al., (2002). The 'p' represents the transitional probability within (1.0) and between (0.33) pairs.

After the habituation, infants were presented with 6 test trials of familiar and novel sequences in alternation. The familiar sequence contained the same relationship between shapes viewed during the habituation phase, whereas in the novel stream each shape was showed in a random order, resulting in a transitional probability equal at 0 across shapes. All groups of infants looked more at the novel stimuli than at the familiar ones, providing evidence that they were able to extract the statistical structure from the habituation sequence. Visual SL ability has been more recently investigated in 1-3-day-old newborn infants by Bulf, Johnson, and Valenza (2011). Following the same procedure used by Kirkham et al. (2002), half of the newborns was habituated to a statistically structured sequence of 6 shapes (HDC= high demand condition), while the other half was habituated to a sequence of 4 shapes (LDC= low demand condition, Figure 1.3).

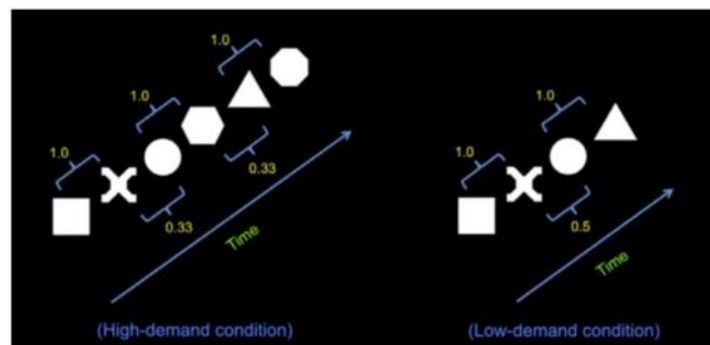


Figure 1.3: A schematic representation of the sequences used in Bulf et al. (2011) to investigate the presence of visual SL abilities at birth.

Results showed that newborns were able to extract the statistical structure of the sequences only in the LDC, whereas in the HDC their performance dropped to the chance level. The author suggested three reasons to explain the results. First, the sequences used during the LDC, composed only by 4 shapes, could be easier to process, because the amount of information that had to be represented and stored in visual short-term memory was reduced. Therefore, memory limitations may act as filter on the input focusing the learning on just a subset of the data (4 elements). Second, the difference in performance between the HDC and the LDC may be linked to the frequency of occurrence of each shapes pair. In low and high demand conditions the TP and co-occurrence frequency perfectly co-varied, even though, in LDC the 4 items have higher frequency of appearance than 6 shapes (HDC) within the same time window. Therefore, it is possible that the redundant TP and co-occurrence frequency

cues had facilitated infants' learning. The third hypothesis take in consideration cognitive limitations of the human neonate that may have reduced the amount of information acquired as well as their limited selective attention capacities. On this account, detection of statistical regularities was possible only when a reduced number of elements composed the learning sequence, facilitating identification of relevant visual information.

In line with Bulf and colleagues (2011), several studies have reported that infants' SL is strongly constrained by the characteristics of the stimulus material. For example, Addyman and Mareschal (2013) ran a modified version of Kirkham et al.'s (2002) experiment, without the habituation phase and using looks away as the dependent measure. Results showed that 5-months-old looked away more when the sequences presented followed a structure in which the shapes were repeated than when the structure was random. The author suggested that infant's preference for random (less number of looks away) versus structured sequences of shapes may not have reflected segmentation based on TP statistics, but could be an effect of attentional deployment. In line with this account, Kidd, Piantadosi and Aslin (2012, 2014) investigated whether and how stimulus complexity modulated infants' SL abilities. The authors exposed infants to auditory and visual sequences in which the complexity changed based on the predictability between the events. In line with their predictions, infants looked away when the events were characterized by very low or very high complexity, showing a preference to look at the stimuli with an intermediate complexity. This finding suggests that the attentional deployment requested by the complexity of the task has direct implications on the functioning of auditory and visual SL during early infancy (see also Saffran and Kirkham, 2017).

Besides stimulus material, infants' SL seems to be modulated by the age of the learner. Marcovitch and Lewkowicz (2009) investigated infants' ability to extract transitional probability and frequency of co-occurrence from visual shape pairs, finding that 2-months-old infants failed to track both transitional probability and frequency of co-occurrence, while 5 and 8-months old infants were sensitive to either types of information. The authors suggested that the sensitivity to frequency of co-occurrence emerges first in the development, and that it provided a basis for the subsequent ability to track transitional probabilities. Slone and Johnson (2015) in another study reported the same results, but they suggested that attentional limitations related to age could play a role in the younger infant's inability to process both computations. The interpretation that SL ability could change during the development is also sustained by a recent study on visual and auditory SL ability in childhood and adulthood that revealed that visual SL ability improve with age (Raviv and

Arnon, 2016). These findings highlight the need to further investigate the age-related changes during the development, along with the role of attentional processes in modulating SL ability during early infancy.

Another important perceptual aspect that modulates infants' SL ability is the spatial and temporal direction embedded in the sequences. For example, in the real word language structure embedded in the utterances requires the ability to track the relative position of the words in the sentence (Mintz, 2002, 2003; Mintz, Newport and Bever, 2002). In this case, the temporal information, i.e., the backward and forward direction of the stimuli, is crucial to parse the sequences. Similarly, in motion perception and the actions production, it is relevant to understand when and where they should be performed, conferring an important status to temporal but also to spatial information (Roseberry, Richie, Hirsh-Pasek, Golinkoff and Shipley, 2011). Based on these characteristics of the auditory and visual stimuli respectively, it is possible to hypothesize that the ability to track statistical probability can differ when computed to backward (i.e., Y preceded by X) and forward direction (i.e., X followed by Y) based on modality specific constraints. Starting from this idea, it has demonstrated that both infants and adults are sensitive to statistical regularities defined in the backward as well as the forward direction when auditory sequences are presented (Jones and Pashler 2007, Pelucchi, Hay, and Saffran, 2009; Perruchet and Desauty, 2008). On the contrary, 8-months-old infants are able to track the predictive direction only in the temporal sequences, but not in spatial configurations (Tummeltshammer, Amso, French, and Kirkham, 2017). These data confirmed the hypothesis that the computations performed by learners are modulated by specific characteristics of the input.

Overall, the studies reported above demonstrated that infants' SL is a flexible mechanism even though it operates under certain constraints, such as the age and the attentional and memory resources of the learners, the characteristics of the to-be-learned material, and the modality (temporal vs. spatial) under which sequences were presented (for a review see Frost, Armstrong, Siegelman, and Christiansen, 2015). Moreover, these findings demonstrated SL is one of the core mechanisms that allow to catch environmental regularities. However, in addition to SL ability, a line of research suggests that infants are equipped with another mechanism that allows them to extract regularities beyond the surface information and to generalize these regularities to novel elements (Marcus et al., 1999). This mechanism, called rule learning, will be described in the next section of this chapter.

Rule learning

Rule learning (RL) is an implicit learning mechanism that is present since early infancy and refers to the ability to detect high-order rules (ABB/ABA/AAB) from a sequence of elements and to generalize them to novel stimuli (Marcus et al., 1999).

Marcus and colleagues (1999) familiarized 7-months-old infants for 2 minutes with a string of syllables that followed an ABB, an AAB, or an AAB rules. During the test phase, infants were presented with a familiar and a novel sequence instantiated by a new set of stimuli, never shown in familiarization phase. Results showed that infants were able to discriminate the novel from the familiar rule at test, providing evidence that they were able to detect and create a mental representation of the high-order rule underlying the presentation of the stimuli and to generalize it to novel elements. This seminal study gave rise to interest debate concerning the language-specific nature of this mechanism. To investigate this issue, Marcus, Fernandes and Johnson (2007) tested 7-months-old infants with the same procedure adopted in the Marcus et al.'s (1999) study, but presenting non-linguistic sequences of sounds (piano notes, musical tones and animal sounds). The authors found that infants successfully detected and generalized the rule to linguistic and sounds stimuli, for this latter only if the infants first heard the rule instantiated in sequences of linguistic elements. However, Saffran, Pollak, Seibel, and Shkolnik (2007) have demonstrated that 7 months old infants can learn sequential rules from visual stimuli that they can readily represent and categorize, such as images of dogs or cats. The authors argued that, instead of being evolved to subserve language learning, rule learning could be considered as a more general mechanism that is modulated by the familiarity of the stimuli to be learned: familiar stimuli, no matter whether they belong to linguistic or visual domains, enhance infants' ability to detect and generalize rules. This idea has been further confirmed by a recent study that demonstrated that infants can easily detect high-order rules from a sequence of faces (Bulf, Brenna, Valenza, Johnson, and Turati, 2015). This latter provided evidence that when infants are exposed to sequences of stimuli for which they have already acquired an extensive experience, they are able to detect and generalize the rules embedded in the sequences. Indeed, when the same sequence of faces contained faces presented in an upside-down fashion, infants failed to learn the rule, demonstrating that less-experienced stimuli are not efficient in driving infants' RL ability. In line with this result, Johnson and colleagues (2009) showed that 8-months-old infants were able to extract and generalize a rule from a sequence of unfamiliar geometrical shapes only in the presence of an ABB pattern, i.e. a pattern that is easier to detect than an ABA pattern by

virtue of containing an adjacent repetition. The same pattern of results was obtained presenting 7-months-old infants with sequences of gestures from the sign language, for which they did not have any previous experience (Rabagliati, Senghas, Johnson, and Marcus, 2012). Moreover, Dawson and Gerken (2009) showed that 4-months-old but not 7.5-months-old appeared to learn AAB and ABA generalizations in chord and tone sequences. The authors suggest that this pattern of result could be related to differential experience with language and music coupled with general cognitive differences, resulting in a different encoding pattern. For instance, music and speech are characterized by different levels of complexity, and 7 months-old infants have more experience with speech than 4 months-old infants. Therefore, speech is acoustically more complex than music sound, and older infants are more expertise and, thus, more sensitive to compute fine-grained analysis of units within speech than music sound.

Overall, these studies suggest that infants' RL is constrained by infants' expertise with the to-be-learned material. However, it has recently found that other perceptual factors can constrain infants' RL ability. Bulf, de Hevia, Gariboldi and Macchi Cassia (2017) have measured whether 7-months-old' ability to learn high-order rules as ABB and ABA from visual sequences of unfamiliar geometric shapes was modulated by the spatial orientation of the sequences. A group of infants was presented with the visual sequences displayed from left to right, while for another group the sequences were presented from right to left. Results showed that infants were able to extract both ABB and ABA patterns when the spatial orientation of the stimuli was from left to right, but failed in the right to left orientation. This finding suggests that a left-to-right spatial organization of sequences promotes infants' RL, and this facilitating effect is most probably due to an infants' advantage in processing the left side of the space (de Hevia, Girelli, and Macchi Cassia, 2012). Another perceptual factor that modulate infants' RL ability is the redundancy of the perceptual cues. Frank, Slemmer, Marcus, and Johnson (2009) have demonstrated that RL in infants at 5 months of life is enhanced in the presence of a multimodal (visual and auditory) information, while in the presence of either the visual or the auditory information infants were not able to extract rules.

Recent studies have also investigated the level of abstractness of infants' RL mechanism. Indeed, Endress, Nespore and Mehler (2009) have suggested that AAB, ABB, and ABA not constituted a real case of abstract rule. To explore this hypothesis, Gervain, Macagno, Cogoi, Peña, and Mehler (2008) conduct a series of studies using a NIRS technique, comparing the performance of newborn to detect ABB or AAB or ABA vs ABC (random) rules from auditory linguistic stimuli. This kind of manipulation (i.e. compare AAB

vs ABC) was relevant to allow to explore the processing and learning of each repetition structure separately, independently of the other. The results showed a significantly greater activation in ABB and AAB than ABC patterns in both the left and the right temporal areas and, interesting, the differential response increased over the course of the experiment in the left frontal area. When ABA vs ABC condition was tested, the results not revealed any significant difference patterns of activation. A more recent study (Gervain, Berent, and Werker, 2012) has compared directly the ABB vs AAB rules revealing, also in this case, different patterns of activations. Therefore, newborns could discriminate between early and late repetitions and most important, this discrimination took place in the brain regions responsible for pattern extraction and higher order processing of structure, confirming the existence of an abstract mechanism. Overall, these results suggest that the adjacent repetition is immediately detected and discriminated from the control sequence by an automatic, low-level mechanism. A recent study further confirmed the hypothesis that RL is a mechanism that operate with abstract information, showing that infants are able to generalize complex hierarchical relations too within a structure. Kovacs and Endress (2014) familiarized 7-month-old to an auditory artificial language composed of AAB or ABB ‘sentences’ of three three-syllabic words (Figure 1.4). Following this familiarization, infants were tested on new sentences with new syllables and new words that agreed or violated the sentence pattern learned in the previous exposure (ABB and AAB sentences, Figure 1.5).

Possible sentence types with structure AAB							
sentence structure	A	A	B	⋮	A	A	B
word structure	abb	abb	aba		aba	aba	abb
example	dubaba	lomomo	zavuzza		dubadu	lomolo	zavuvu

Possible sentence types with structure ABB							
sentence structure	A	B	B	⋮	A	B	B
word structure	aba	abb	abb		abb	aba	aba
example	dubadu	lomomo	zavuvu		dubaba	lomolo	zavuzza

Figure 1.4 The hierarchical structures used by Kovacs and Endress (2014).

<i>Sentence structure</i>	<i>Word structure</i>	<i>Sequence</i>
Participant group 1		
AAB	aba-aba-abb	dubadu lomolo zavuvu
AAB	abb-abb-aba	dubaba lomomo zavuza
AAB	aba-aba-abb	lovulo zabaza dumomo
AAB	abb-abb-aba	lovuvu zababa dumodu
AAB	aba-aba-abb	zamoza duvudu lobaba
AAB	abb-abb-aba	zamomo duvuvu lobalo
Participant group 2		
ABB	aba-abb-abb	dubadu lomomo zavuvu
ABB	abb-aba-aba	dubaba lomolo zavuza
ABB	aba-abb-abb	lovulo zababa dumomo
ABB	abb-aba-aba	lovuvu zabaza dumodu
ABB	aba-abb-abb	zamoza duvuvu lobaba
ABB	abb-aba-aba	zamomo duvudu lobalo

Figure 1.5 Test sequences used by Kovacs and Endress (2014).

Results showed that infants discriminated between novel sentences that violated the hierarchical pattern and novel sentences that were conformed to the familiarization pattern, looking much longer the violating than conforming structures. Additionally, the results revealed that infants were more sensitive to discriminate structures when the repeated word pattern during test followed ABB than ABA rules. Hence, patterns of syllables based on non-adjacent repetition (ABA) are much harder to learn than patterns characterized by adjacent repetition (ABB), confirming previous evidence finding in visual domain (as in work of Johnson et al., 2009). Even though, it is not clear at which level of the sentence's structure infants learned, this study suggests that infants are able to embed word patterns into a higher-level structure, showing to be able to extract and generalize hierarchically relationship too.

Overall, the studies reported above demonstrated that RL is a domain-general mechanism that operates since the early months of life allowing infants to represent rule-like patterns at an abstract level and to generalize them to new contexts. As already reported for SL ability, RL ability is highly constrained by multi factors, such as infants' expertise with the to-be-learned material, the complexity of the to-be-learned rules, and the presentation of the sequences (spatial orientation and multimodal information).

While, SL and RL seem to share a similar developmental course, these mechanisms are characterized by different proprieties: 1) SL allows to extract transitional probabilities while RL allows to extract and generalize abstract rules; 2) SL has been found from birth whereas RL become evident from the third month of life; 3) respect to SL, RL seems to be much more influenced by infants' expertise with the to-be-learned material. Given these distinct properties of SL and RL, it is suggested that the outputs of these learning processes are distinct too (Endress and Bonatti, 2007; Marcus, 2000; Marcus, et al., 1999).

Implicit learning and individual differences in language, learning and communicative skills

Recently, it has been proposed that implicit learning mechanisms are linked with a wide range of cognitive abilities (Armstrong, et al., 2017; Ullman, 2016) including language (Arciuli and Torkildsen, 2012; Conway and Pisoni, 2008; Gervain and Mehler, 2010; Gogate and Hollich, 2010; Kuhl, 2004; Perruchet and Pacton, 2006; Reber, 1967; Romberg, and Saffran, 2010), and social-cognition (Frith and Frith, 2008; Ruffman, Taumoepeau, and Perkins, 2012). Capitalizing on this view, in the last two decades researches had started to focus on what learning can do for learners (Saffran and Kirkham, 2017), studying how individual differences are linked to the functioning of the implicit learning mechanisms. In this paragraph, I will describe some of the studies that have demonstrated a link between SL and RL abilities and the development of complex cognitive skills, such as linguistic and communicative skills.

The link between implicit learning abilities and language development has been studied with the aim to discover how infants acquired complex language competence. In fact, to achieve language proficiency, infants must parse a speech stream in highly predictable sequences of syllables composing words. Successively, they have to catch the relationship between those words to determine the system of rules that combine the unity of speech. Finally, they have to generalize these rules to new words. However, there are not definitive acoustic cue for word boundaries, and neither for grammatical categories that can help to detect words and syntax structures, respectively.

In literature, researchers have proposed two hypothesis on how learning is involved in language acquisition . One hypothesis suggests that statistical learning is related with speech segmentation, while rule learning is related to the acquisition of the grammatical structure of language (Endress and Bonatti, 2007; Marcus, 2000). Therefore, SL allows to identify isolated words without a prior knowledge about specific sounds (Saffran, 2003), while RL allows to extract linguistic structures such as adjacent and not adjacent relationships between linguistic units. More specifically, RL allows to create an abstract representation of the order of the units in the structure and to generalize this representation to novel words (Kovacs and Endress, 2014; Marcus, 1999). An alternative hypothesis proposed that SL mechanisms played a role in both speech segmentation and grammar acquisition. Following this issue, SL and RL are the part of the same mechanism that allows to extract either the word boundaries and the higher level, grammatical structure of language (for a review see Aslin and Newport,

2012). In this way, humans are equipped with a mechanism ‘sensitive to regularities in the input’ and the application of these regularities on a familiar input (SL) or on novel elements (RL) may represent different outcome of the same process (Endress and Bonatti, 2007; Marcus, 2000).

To date, this debate is still extremely open. Indeed, while a growing body of research has investigated the link between SL and language skills, to our knowledge, no studies have investigated the role of RL mechanism in language acquisition. The research of the link between SL and language has been focused on the adult population (i.e. Arciuli and Simpson, 2012; Daltrozzo, et al., 2017; Frost, Siegelman, Narkiss, and Afek, 2013). Just few studies have investigated this link in childhood and infancy. For example, Arciuli and Simpson (2012) tested the relationship between the ability to track transitional probabilities between visual elements and reading skills in 9 years old children and adults using a familiarization forced choice paradigm. The familiarization phase comprised a continuous stream of triplets of aliens presented one at a time in the center of the screen. The transitional probabilities were high (1.0) within the triplets and low between the triplets of aliens. During the test phase, both adults and children discriminated the familiar sequence from a novel sequence in which the transitional probability was equal to 0. Additionally, separate correlational analysis revealed a positive link between SL ability and reading skills, regardless the children age and grade school. In line with this finding, Kidd & Arciuli (2016) demonstrated that sensitivity to statistical regularities predicts syntax comprehension (i.e., passive and relative clause sentences) in 8-years-old children, showing that a general domain SL ability seems to subserve lexical and grammatical knowledge in children and adults.

Researchers have investigated the relationship between SL and language acquisition in infancy using a longitudinal approach. Shafto and colleagues (2012) tested the relationship between SL abilities, assessed by response times during a visual sequence learning task, and language outcome in 8.5 months-old infants. Infants were exposed to sequences of three unfamiliar elements that appeared in predictable spatial-temporal sequences (i.e., left–center–right). During learning, infants became faster to follow the stimuli within the sequence and, consequently, to anticipate the location of the next element in the sequence. Moreover, results showed that infants who were faster in allocating their gaze on the predictable locations had greater receptive vocabulary size at 13 months, providing evidence that visual sequence learning can predict a specific language skill as vocabulary comprehension. In line with this evidence, Ellis and colleagues (2013) have demonstrated that visual sequence learning can predict the productive vocabulary at 22 months.

Unfortunately, these studies did not investigate the link between early visual learning abilities and later syntax outcome, leaving unresolved the role of SL in grammatical development. Moreover, to the best of my knowledge, no studies have investigated the relation between infants' RL abilities and linguistic development in a longitudinal perspective.

Recently, it has been suggested that implicit learning mechanisms are crucial also for the development of social and communicative skills. Research on this account is still scarce and, to our knowledge, no studies have investigated the link between early SL and RL abilities and later social and communicative skill using an individual differences approach. However, a recent model has tried to explain the link between implicit learning and actions understanding. This could be helpful to better understand the deficit reported in ASD. As language is composed by units, even mental state and goal predictability are supposed to be composed by structured behavioural patterns. To this end, it has been proposed that infants could segment goal-directed behaviours in sub-component action's units based on the sequential predictability of the action observed (Stahl, Romberg, Roseberry, Golinkoff, and Hirsh-Pasek, 2014). The ability to segment a continuous flux of actions into units seems to be important for the development of social skills, as this ability allows to anticipate future actions and to create a hierarchical representation of events. This representation, in turns, is critical for the development of a theory of mind (Ruffman et al., 2012). On this account, Stahl and colleagues (2014) tested the ability of infants at 7 and 9 months of age to segment a continue flux of events. The stimuli consisted of a purple animated starfish with eyes performing a set of actions (i.e. bow, clap, jumping). Each action was composed by five unit's movement comprising the starting and the final positions, and the transitional probabilities within each unit were high (1.00) that between units (0.5). Importantly, the actions and units were equated in the frequency with which they occurred. During the test phase, infants successfully discriminated between actions with a transitional probability of 1.00 and part-unit actions in which the transitional probability was 0.50, revealing that infants were able to segment the continuous stream of actions based on the statistical relationships of the elements of the sequence. A recent study by Monroy, Meyer, Gerson, and Hunnius (2017) further explored this matter, providing evidence that both adults and infants were able to segment continuous action streams into discrete events using statistical cues when actions were also performed by two actors that co-operated. In line with these evidences, it seems that SL is involved in understanding intentions behind goal-directed behaviours (Ahlheim, Stadler, and Schubotz, 2014; Baldwin, Baird, and Saylor, 2001; Stahl et al., 2014).

Statistical and rule learning abilities in language, learning and communicative developmental disorders

An approach related to the study of individual differences in sequential learning abilities involves the study of these mechanisms in children and infants that presented respectively a diagnosis or a familiar risk for language, learning and communicative disorders, i.e. specific language impairments (SLI), developmental dyslexia (DD) and autism spectrum disorders (ASD). Even though, these deficits present different types of phenotypes, an overlap of clinical behaviors has been reported (Bishop, 2002; Tomblin, 2011). For example, both DD and SLI are characterized by phonological deficits (Ramus, Marshall, Rosen, and van der Lely, 2013), and more than 50% of children with SLI may develop reading problems similar to those seen in individuals with dyslexia (Bishop and Snowling, 2004). In addition, children with a diagnosis of SLI and ASD are both characterized by poor spoken communication skills and several studies have described an increased prevalence of language delay and language-based learning deficits in parents and siblings of autistic individuals (Tomblin, 2011). Given the high rate of co-morbidity, and evidences of common genetic susceptibility (Bishop, 2010; Pennington and Bishop, 2009; Eicher, and Gruen, 2015), SLI, DD and ASD might share an impairment in underlying neuropsychological mechanisms linked to language and communication disorders.

Some evidences account for the possibility that an impairment in implicit learning mechanisms play a crucial role in the emergence of the deficits found in these clinical populations (for a review see Ullman 2004, 2016). The declarative/procedural model assumes a categorical distinction between lexical and grammatical knowledge, proposing that a procedural memory mechanism is impaired in these populations despite a spared declarative memory system (Ullman and Pullman, 2015). The declarative memory system, that is rooted in temporal lobe structure, is viewed as the responsible for learning representation, and knowledge about facts (semantic memory) and events (episodic memory). In the linguistic domain, implicit learning mechanisms has been proposed to be crucial for the acquisition and representation of mental lexicon, such as idiosyncratic linguistic knowledge, their phonological forms, categorization knowledge, irregular words and lexical and semantic knowledges. The procedural memory system, that is rooted in frontal/basal-ganglia structure, is involved in the acquisition of motor and cognitive skills, without awareness. Moreover, it has proposed that procedural learning might be relevant in language processing, as it allows computing the rule-based procedures, defined as learning of sequential representations that

are characteristic of syntax and even morphology and phonology (Ullman, 2004, 2016; Ullman and Pierpont, 2005). In this way, the impairment in grammar, phonology, morphology and even motor skill found in SLI, DD and ASD could be explained by an impairment in procedural system, despite an intact lexical knowledge related to an intact declarative memory system (see a review: Ullman and Pullman, 2015).

The functioning of implicit learning mechanisms in these developmental disorders has been investigated by several studies. For example, Evans, Saffran, and Robe-Torres (2009) examined the ability to track statistical relationships embedded in auditory sequences in two groups of children with a typical development and with a diagnosis of SLI. In a first experiment, each group was familiarized for 21 minutes with a speech string in which transitional probabilities were higher within words than across words boundaries. During the test phase, children heard words containing the same transitional probability listened during the familiarization phase and a new set of non-words in which the transitional probability between syllables was 0. In a second experiment, using the same design, children were familiarized with a string of words for 42 minutes and a string of musical sound for 42 minutes following the same statistical structured of previous study. Results showed that while the control group was able to extract the transitional probabilities embedded in the sequences in all the experimental conditions, the SLI group was able to extract transitional probability only when exposed to the sequence for 42 minutes and only in the speech condition. Moreover, in both the control and the SLI groups the performance at the SL task correlated with the receptive vocabulary. These findings revealed that children with SLI presented a less efficient SL mechanism respect to typically developing children. More recently, it was found that auditory SL correlated with lexical-phonological skills but not with lexical-semantic knowledge (Mainela-Arnold and Evans, 2014), confirming that the procedural and declarative memory systems are linked to different lexical learning in SLI.

The declarative/procedural model seems to be less consistent in explaining the deficits in DD and ASD respect to SLI. For example, the core deficit in DD is a poor phonological ability (Snowling, 2001), likely arising from a deficit to manipulate and retrieval phonemic knowledge saved in declarative memory system. For the declarative/procedural model, the declarative memory system is supposed to be intact in DD (Ullman, 2004). However, an impairment in procedural memory system may cause sensory-motor difficulties observed in this population that may be related to an impoverished representation of the phonological knowledge. This, in turn, might lead to a concomitant deficit in grapheme-phoneme conversion, and words recognition (Nicolson and Fawcett, 2011). It has been also proposed

that an impairment in SL abilities, related to the creation of phonological representation, may explain the reading problem in DD in conjunction with sensory motor difficulties. For example, Gabay, Thiessen and Holt (2015) investigated SL ability using speech and non-speech (musical tone) sequences of stimuli in individual with diagnosis of DD and in a non-diagnosed control group. In the speech conditions, the participants were exposed for 2 minutes to a continuous speech stream consisting of four three-syllable nonsense words (i.e., *tupiro*, *golabu*, *bidaku*, *padoti*) repeated in random order, in which the transitional probability between syllables pairs within words was higher than across words. After the familiarization phase, participants completed a force-choice test composed by eight trials in which words (high probability) and part-words (low probability) were presented. The participants were requested to judge which of the two stimuli, words and part-words, were more familiar to the stimuli previously heard during familiarization phase. The same procedure was used with the non-speech sequences. Results showed that adults with DD performed more poorly on speech and non-speech SL tasks than non-diagnosed control group. Additionally, a significant correlation was found between the ability to learn the statistical regularities in both the speech and non-speech sequences. The participants' reading ability, further confirmed the role of implicit learning system in some aspects of reading profile in DD. To our knowledge, only one study has investigated the ability to track non-adjacent dependencies in infants at family risk for DD (Kerkhoff, De Bree, De Klerk, and Wijnen, 2013). Using a head turn paradigm, infants with a family risk for DD and typically developing infants were exposed to an artificial language composed by string of three pseudo-words in non-adjacent dependencies. Specifically, the string contained the dependencies a-X-c and b-X-d, in which the first element predicted the last one and the middle X element continuously changed within the same string (i.e., *tep wadim lut*, *tep kasi lut*; *sot wadim jik*, *sot kasi jik*). During the test phase, infants listened to familiar (a-X-c, b-X-d) and novel (a-X-d, b-X-c) structures. The control group showed more interest to the novel than to the familiar structures, revealing that they were able to extract the non-adjacent relationship embedded in the sequences. On the contrary, infants at risk for DD were unable to track these dependencies. This finding indicates that infants at family risk for DD have a deficit in learning non-adjacent dependencies, a disability that might affect the subsequent development of phonological skills.

The role of implicit learning mechanisms has been recently investigated also in ASD. Mayo and Eigsti (2012) investigated the ability to extract transitional probabilities from a string of auditory stimuli in high-functioning autistic children and in typically developing

children (7-17 years). The paradigm and materials were the same used in the Evans et al.'s (2009) study for SLI. Results showed that the ASD group and the control group were equally able to discriminate between structured and random sequences of linguistic elements, revealing an intact ability to track transitional probabilities. In contrast, using the fMRI technique, Scott-Van Zeland and colleagues (2010) found that children with ASD (9-16 years) showed a different pattern of cortical response compared to control group. Differently from Mayo and Eigsti (2012), this latter finding was obtained using neuroimaging techniques as implicit measure of the SL ability, accounting for the importance of assessing SL in ASD through a procedure that avoided the use of top-down (explicit) compensatory strategies. In line with this approach, more recently, Jeste, et al. (2015) recorded electrophysiological response during the exposure to continuous string of visual stimuli in children with ASD (high and low functioning) and in typically developing children (2-6 years). In this study, an oddball version of the paradigm implemented by Kirkham and colleagues (2002) was used. Children were familiarized with three pairs of shapes presented in random order. Therefore, the first shape of the pair always predicted the next element (1.0 of probability), while the predictability across pairs were low (0.33). After the familiarization phase, children looked a string shapes in which 90% of trials contained the same predictability between shapes shown during familiarization, while in the 10% of the trials shapes predictability was 0. In contrast to the control group, the ASD group showed a reduced evidence of defined as N1 and P300 components. Moreover, a positive correlation between statistical ability and non-verbal IQ and adaptive social function was found. This finding highlights that SL ability could be impaired in children with ASD and that a specific deficit in visual SL mechanisms could have a cascading effect on the development of social and adaptive behaviors rather than on language skills. This is the only study that has investigated visual SL in children with ASD.

Therefore, more research is needed to better explain the role paly by visual SL in social and communicative skills (chapter 5).

Conclusion

The present chapter reports some of the studies that have investigated the development of SL and RL mechanisms in early infancy, their capacity of explaining the individual differences in linguistic outcomes, and their role in the development of SLI, DD and ASD neurocognitive disorders. Overall, these findings suggest that the declarative/procedural model has a considerable explanatory power to define both typical and atypical language development (Ullman, 2004).

CHAPTER 2

RESEARCH QUESTIONS AND GENERAL AIMS

The procedural/declarative model hypothesized that implicit learning mechanisms underlie a wide range of complex abilities as language, learning and communication skills (Ullman, 2004; 2016) and it converges with the neuroconstructivist model to the study of typical and atypical development (Karmiloff-Smith, 1998). Indeed, the neuroconstructivist model posits that complex cognitive abilities, such as language and social cognition, emerge gradually during the development as the result of a complex and continue interaction between different levels, e.g. gene, cognitive processes and environment. This model has crucial implications also for the way in which atypical development is considered, as it proposes that tiny variations in the initial state of the organism might cause a cascading effect on the developing system, resulting in distinct clinical outcomes later in development. On this vein, both the procedural/declarative and the neuroconstructivist models encourage the study of early markers for later neurocognitive disorders for early diagnosis and treatments.

The aim of the present thesis was to investigate whether implicit visual statistical learning (SL) and rule learning (RL) abilities are related to linguistic and communicative outcomes in typical and atypical development, i.e. in specific language impairment (SLI), developmental dyslexia (DD) and autism spectrum disorder (ASD). To this end, we use four different approaches: 1) the study of typically developing infants; 2) the study of diagnosed children; 3) the study of infants at low risk to develop these disorders by virtue of having parents with sub-threshold high traits; 4) the study of infants with a family risk to develop these disorders defined as having a first degree with a certified diagnosis. We tested SL and RL abilities in the visual domain, using unfamiliar geometrical figures, to remove any learning biases due to individual differences in the expertise acquired with human speech. Moreover, the majority of the researches reported in this thesis have focuses on the study of visual RL mechanism. Indeed, while a wide body of research have investigated the relation between SL and the development of linguistic and communicative skills, to my knowledge no studies have investigated the role of RL in typical and atypical language outcomes.

My PhD research project is part of a broad longitudinal study that is carrying out at the IRCCS ‘E. Medea’ (Bosisio Parini, Lecco) with the aim to investigate the early markers for SLI and DD in a multi-factorial prospective (Cantiani et al., 2016). For the sake of

brevity, in this thesis I will report only part of the studies that I have carried out in the last three years of my PhD (see Table 2.1).

The first study that I will present (chapter 3) had the aim to investigate whether visual RL abilities in typically developing preverbal infants can predict later linguistic outcomes. Indeed, while it has been widely proposed that infants' RL abilities are linked to the extraction of the grammatical structure of language (Endress and Bonatti, 2007; Marcus, 2000; Marcus et al., 1999), to date no studies have directly investigated the presence of this link. Indeed, while it has been demonstrated that infants can extract and generalize high-order rules (Gervain et al., 2012; Marcus et al., 1999) and even hierarchic patterns from linguistic stimuli (Kovacs and Endress, 2014), the role of RL in language development is still unexplored. Using a visual habituation procedure, we assessed whether visual RL in 7-months-old infants was related to their vocabulary and grammatical development at 2 years of age. Language outcomes were measured by the parental-report questionnaire called 'Primo Vocabolario del Bambino (PVB), Parole e Frasi' (Caselli and Casadio, 1995). We expected that visual RL was a predictor of infants' grammatical development. Conversely, we did not expect a link between visual RL and vocabulary development.

Using the same approach, we are currently investigating the link between visual SL ability in 7-months-old infants and their linguistic outcome at 2 years of age. Moreover, in collaboration with the baby lab of the University of California Los Angeles (prof. Scott P. Johnson), we are testing 9- to 15-months-old infants' ability to learn multi-layered visual structures in which infants should extract SL and RL information within the same task. This latter study is crucial for the understanding of the specific role of SL and RL information in driving infants' learning of complex sequences (see Table 2.1).

The second study (chapter 4) investigated the functioning of visual RL in 8- to 10-years-old children with a diagnosis of DD. As previously reported (chapter 1, paragraph 1.4), DD is characterized by phonological deficits but also by morpho-syntactic and syntactic impairments (Cantiani, Lorusso, Perego, Molteni, and Guasti, 2013a; Cantiani, Lorusso, Guasti, Sabisch, and Männel, 2013b; Guasti, Branchini, Vernice, Barbieri, and Arosio, 2015). The procedural/declarative model by Ullman (2004) posits that reading and language deficits found in DD might be caused by a common impairment in implicit learning mechanisms. Recently, it has been reported that adults with DD have a difficulty in the extraction of statistical relationships from speech and non-speech sequences, and that this deficit is linked to a poor phonological representation (Gabay et al., 2015). On the contrary, to our

knowledge, no studies have directly investigated the role of RL abilities in DD. As RL is considered to be linked to grammatical development, we hypothesized that a deficit in RL could explain the specific syntactic and morphotactic deficits that characterized this population. Using a modified version of the visual RL paradigm developed by Bulf and colleagues (2017), we compared visual RL abilities in DD and typically developing children. Moreover, we correlated children's performance in the visual RL task with their cognitive, linguistic and reading abilities assessed through standardized tests.

Using the same approach, we are also investigating the functioning of visual RL ability in high functioning autistic children (see Table 2.1).

The last two studies will focus on the functioning of SL and RL mechanisms on infants at risk to develop ASD, SLI and DD. SL and RL abilities are perfect candidates to investigate early markers in these disorders as: 1) these mechanisms seem crucial to develop complex cognitive abilities, 2) are present since the first months of life, 3) can operate in the visual domain. In the third study (chapter 5) we investigated visual SL abilities in 7-months-old infants whose parents showed high and low autistic traits. The most frequent approach to investigate early markers for ASD is the study of infant siblings of children with autism, as siblings are part of a broad autism phenotype in which ASD represents the upper extreme of a constellation of traits continuously distributed in the general population (CIT.). However, neurocognitive deficits underlying social and communicative impairments in ASD can also found in individuals from the general populations that showed high autistic traits (Hudson, Nijboer and Jellema, 2012). Since autistic traits are high heritable (Robinson et al. 2011; Ronald, and Hoekstra, 2011), we investigated visual SL ability in infants of (non-diagnosed) adults who show a different degree (high vs. low) of autistic traits. As visual SL abilities are impaired in children with a diagnosis of ASD (Jeste et al., 2015; chapter 1, paragraph 1.4), we hypothesized that infants whose parents had high autistic traits would show a difficulty in visual SL abilities respect to infants whose parents had low autistic traits.

Finally, in the last study (chapter 6) we investigated the functioning of SL and RL in 7-8-months-old infants with a family risk to develop SLI and DD by virtue of having a first-degree relative with a certified diagnosis. As already reported in chapter 1 (paragraph 1.4), SLI and DD seem to share common linguistic deficits and genetic susceptibility that results in most case in an overlap between these two disorders (Bishop & Snowling, 2004). For example, an impairment in phonological and syntax skills (Ramus et al., 2013), as well as an impairment in the ability to track statistical relations across auditory stimuli (Evans et al, 2009; Gabay et al., 2015), has been found in both SLI and DD. Using a visual habituation

procedure, we investigated visual SL and visual RL abilities in a group of infants at risk to develop SLI and DD and in control group of no-risk infants. We expected that at risk infants would show an impairment in visual SL and RL abilities respect to the control group.

	AIM OF STUDY	POPULATION	TYPE OF STUDY	AGE, N SAMPLE	STAGE	INSERTED (in the thesis)
Typically developing infants	Investigating if visual SL and RL abilities can predict specific aspect of language ability	TD infants	Longitudinal study	Step 1: 8-month-old infants Step 2: 24-month-old infants • N = 27	Completed	YES
		TD infants	Longitudinal study	Step 1: 8-month-old infants Step 2: 24-month-old infants • N = 14	Ongoing	NO
Diagnosed children	Investigating if infants are able to learn multi-layers visual sequences	TD infants	-	Age: 9-15-month-old infants • N = 20	Ongoing	NO
		Children with DD	Comparison between two groups	Age: 8-11-year-old children • TD children, N = 19 • DD children, N = 18	Completed	YES
Infants at risk	Investigating if faces modulate visual RL abilities in ASD	Children with ASD	Comparison between two groups	Age range: 14-18 years old • TD children, N = 12 • ASD children, N = 10	Ongoing	NO
		Infants at high risk for SLI and DD	Comparison between two groups	Age: 7- and 8-month-old infants • TD infants, N = 20 • Infants at risk, N = 10	Ongoing	YES
	Investigating visual SL as an early marker for ASD	Infants at low risk for ASD	Comparison between two groups	Age: 7-month-old infants • Low autistic traits group, N = 20 • High autistic traits group, N = 20	Completed	YES

*TD= group of individuals with typical development.

Table 2.1 Schematic representation of the studies carried out during my PhD.

CHAPTER 3

VISUAL RULE LEARNING AT 7 MONTHS OF AGE PREDICTS LANGUAGE OUTCOME AT 2 YEARS

This chapter will report a study that investigated whether visual rule learning (RL) – defined as ability to detect high order rules from a sequence of elements and to generalize them to new stimuli (Marcus et al., 1999) – can act as an early predictor of later grammatical development. While Marcus and colleagues (1999) proposed that infants’ RL is closely related to infants’ ability to learn the grammatical structure of language, no studies have empirically investigated the presence of this link. Using a longitudinal design, we first investigated visual RL abilities in 7-months-old infants. We then measured their linguistic (vocabulary and grammatical) outcomes at 2 years of age.

This chapter is adapted from:

Bettoni, R., Riva, V., Cantiani, C., Molteni, M., Macchi Cassia, V., and Bulf H. (under submission). Implicit learning of visual structural regularities at 7 months predicts language outcome at 2 years.

Introduction

Language is a fundamental and complex cognitive human ability containing several levels of structures, from the order of syllables within words to the order of words that build utterances. Starting from the last trimester of gestation, infants approach the complex task of language learning equipped with a set of neuropsychological and perceptual abilities that allow them to organize and give meaning to the linguistic input (Saffran et al., 1996). These include domain-general cognitive mechanisms such as implicit learning, that is the ability to exploit statistical dependencies in the environment in order to generate knowledge representations without intention or awareness of what has been learned (e.g., Reber, 1967).

Implicit learning is not a unitary construct. Indeed, different kinds of learning mechanisms fall under the broad umbrella of implicit learning; statistical learning and rule learning are two examples (for SL: e.g., Saffran et al., 1996; for RL: e.g., Marcus et al., 1999). Statistical learning (SL) refers to the ability to extract structural relations defined by statistical regularities from a continuous stream of visual or auditory input (Saffran et al., 1996), while rule learning (RL) allows infants to detect abstract rule-like patterns defined by item repetitions and to generalize them to new exemplars that may have no surface features in common with those on which learning took place (Marcus et al., 1999). These mechanisms are functional from the earliest stages of development (e.g., Bulf et al., 2011; Gervain et al., 2008; Marcus et al., 1999; Saffran et al., 1996), and are domain-general in nature, as they operate on both auditory – i.e., linguistic and non-linguistic – and visual input (e.g., Dawson and Gerken, 2009; Johnson et al., 2009; Kirkham et al., 2002; Saffran et al., 2007).

SL and RL are both seen as pivotal to language acquisition and the development of early communicative skills (Aslin and Newport, 2014; Lieberman, 2000; Perruchet and Pacton 2006; Romberg and Saffran, 2010). In particular, it has been proposed that the processing of statistical dependencies is critical to speech segmentation and vocabulary acquisition (e.g., Perruchet and Pacton, 2006; Saffran et al., 1996), whereas infants' ability to learn rules hidden in environmental stimulation is seen as critical to the extraction of the grammatical structure of linguistic input (e.g., Endress & Bonatti, 2016; Marcus et al., 1999; Peña, Bonatti, Nespor, & Mehler, 2002). One approach to the investigation of the relation between implicit pattern learning abilities and language acquisition has been to perform longitudinal prospective studies relating infants' SL to later vocabulary skills. For example, Shafto and colleagues (2012) showed that the ability to learn visual sequences at 8 months predicts vocabulary comprehension at 13 months, and a similar relation was found between

visual sequential learning at 6 months and receptive and productive vocabulary at 22 months (Ellis et al., 2014). On the other hand, the impact of early RL ability on language acquisition has not been empirically explored.

In the current study, we aimed to fill this gap by exploring whether the ability to learn abstract rules embedded within sequences visual items at 7 months of age predicts grammatical and/or lexical development at 2 years of age.

RL was first investigated by Marcus and colleagues (1999) by presenting 7-months-old infants with a sequence of syllables that contained repetition-based rules such as ABB (i.e., *wofefe*), ABA (i.e., *wofewo*), or AAB (i.e., *wowofe*). After 2 minutes of exposure, infants were able to generalize the rule to novel syllables, showing that they had detected and recognized the rule acquired during the learning phase. Under similar testing conditions, infants failed to show evidence of learning rules instantiated over non-speech sounds, although they showed generalization to non-speech stimuli of rules acquired from speech (Marcus et al., 2007). Moreover, 7-months-old infants succeeded in learning and generalizing rules from non-speech tones that were presented within the context of a natural conversation between two human agents (Ferguson and Lew-Williams, 2016). On the same line, it has been shown that redundant multisensory information delivered by social touch (i.e. touch sequences received from the experimenter) modulates infants' learning of tone patterns (Lew-Williams, Ferguson, Aby-Zhaya, and Seidl, 2017).

Overall, these findings were interpreted as indicating that RL in the auditory perceptual domain is enhanced by communicative and social signals, which enhance infants' attentional engagement and thus their ability to detect underlying structure (Ferguson et al., 2016). However, there is now ample evidence that, in infancy, RL mechanism is fully operative in the visual domain as well, even in the absence of social cues. Several studies showed that, at 7 months, infants can extract and generalize high-order rules not only from visual sequences composed of realistic images of familiar objects, such as dogs (Saffran et al., 2007) or upright faces (Bulf et al., 2015), but also from sequences of artificial geometrical shapes (Bulf et al., 2017; Johnson, et al., 2009). Overall, these evidences show that RL in infancy is a domain-general mechanism that operates across different perceptual domains.

By adopting a longitudinal approach, in the current study we empirically explored the potential role of early RL mechanism in the extraction of the grammar structure of language (Endress and Bonatti, 2016; Marcus, 2000; Marcus et al., 1999, Peña et al., 2002). Learning the grammar structure embedded in the utterances requires the ability to keep track of the relative position of the words in the sentence (Mintz, 2002, 2003; Minzt et al., 2002), and to

generalize this information to novel linguistic elements. Indeed, this is exactly what infants do when they extract the rule delivered by the invariant positional relation of the items within visual or auditory sequences, and generalize such rule to novel items. However, to our knowledge, no studies attempted to investigate whether RL abilities in infancy predict later linguistic outcome, and specifically grammar skills. In the present study, RL was assessed as the ability to learn abstract rules involving adjacent and non-adjacent repetitions of visual items. Testing RL mechanisms in the visual perceptual domain allowed us to remove any bias due to the nature of the linguistic stimuli, and thus further investigate the relationship between domain-general abilities and later language acquisition (Hollich, Hirsh-Pasek, and Golinkoff, 2000, Karmiloff-Smith, 1998).

The present study is a longitudinal follow-up of an earlier study by Bulf and colleagues (2017) in which 7-months-old infants detected and learned rules specified by adjacent-late (ABB) and non-adjacent (ABA) repetitions of one element in three-item sequences of geometrical shapes presented sequentially on the screen from left to right. Unlike earlier studies where visual sequences were presented centrally on the screen (Johnson et al., 2009), infants in Bulf et al.'s study succeeded in learning and generalizing even the ABA rule, which is considered more complex than the ABB rule, as it involves non-adjacent repetitions of the A element. The study included also a second condition, in which visual sequences were presented with a right-to-left spatial orientation, and infants failed to show any evidence of RL abilities. Therefore, the main finding of Bulf et al. (2017) showed that visual RL ability at 7 months are boosted by the directional, left-to-right spatial orientation with which visual information is provided.

Based on this evidence, here we performed a longitudinal follow-up of the infants tested by Bulf et al. (2017) at 7 months in the left-to-right spatial orientation condition in order to test RL as a possible predictor of grammar skills, as opposed to lexical skills. Language skills at 24 months were assessed through the parent report questionnaire 'Primo Vocabolario del Bambino (PVB), Parole e Frasi' (Caselli & Casadio, 1995), which is the Italian version of the 'MacArthur-Bates Communicative Development Inventories (CDI): Word and Sentences' (Fenson et al., 1993). The mean length of utterances (MLU) and the number of words produced (Vocabulary) were collected as measures, respectively, of grammar and lexical skills. The relation between each of these measures and RL ability exhibited by the same infants at 7 months of age was investigated by means of correlation analyses; we expected that, if the ability to extract abstract rules from sensory input is critical to learning the grammatical structure of language, infants' visual RL skill should exhibit a

significant positive correlation with MLU measures, in the absence of specific relations with vocabulary.

Methods

Participants

The sample included 27 7-months-old infants (18 females; mean age = 7 months and 12 days; range = 7 months - 7 months and 29 days) who participated in Bulf et al.'s (2017) study, for whom data collection on language skills at 24 months (mean age = 24 months and 7 days; range = 24 months - 24 months and 18 days) was successful. All infants were healthy and full-term and were monolingual as their parents were both native Italian-speakers. For all infants, first degree relatives had no certified diagnosis of specific language impairment or learning disability. The procedure was approved by the Ethical Committee of the University of Milano-Bicocca.

Procedure

Infants' rule learning task

The stimuli and procedure used to test infants' RL abilities are described in Bulf et al. (2017). Twelve unique coloured shapes presented on a grey background were used as stimuli. When viewed from a distance of 60 cm, each shape was embedded in a virtual square of $10^\circ \times 10^\circ$ visual angle. The shapes were organized in triplets following an ABB (repetition of the same element B in the last position) or an ABA (not adjacent repetition of the A element) rule. Eight unique shapes were presented during habituation, and four different unique shapes were presented during the test phase. For the habituation triplets, four shapes were assigned to the A group and four to the B group. These were randomly combined by the software to create 16 different ABB sequences and 16 different ABA sequences. For the test triplets, two shapes were assigned to the A group and two to the B group, and the software randomly combined them to create 4 different ABB sequences and 4 different ABA sequences. Each triplet was shown one at a time on the screen, and the images within each triad were presented sequentially from left to right. The first image was displayed on the left side of the screen for 330 ms, the second image was displayed in the middle of the screen for 330 ms, and the third image was displayed on the right side of the screen for 830 ms. The distance between the centre of each image was 16° of visual angle. The triplets were presented in a random order

and were separated by a 500 ms blank screen. Half of the infants were randomly assigned to the ABB habituation condition, the other half to the ABA habituation condition (Figure 1).

Infants were tested with an infant-controlled habituation procedure. Each trial began as soon as the infant fixated a cartoon-animated image associated to a varying sound, which appeared in the centre of the screen. Each trial consisted of triads of images organized in either the ABB or ABA pattern. The experimenter recorded infant’s fixation by holding the mouse button whenever the infant fixated on the stimulus. Each trial continued until the infant looked continuously for a minimum of 500 ms and ended when the infant looked away for 2 consecutive seconds or looked for a maximum of 60 s. The habituation phase ended when the infant saw a maximum of 25 trials or met the habituation criterion, which was defined as a 50% decline in looking time on three consecutive trials, relative to the looking time on the first three trials. Following habituation, infants viewed 6 test trials in which triplets of novel shapes instantiating the ABA and ABB rules were presented alternately, each for three times, with half of the infants seeing the triplet instantiating the familiar rule first.

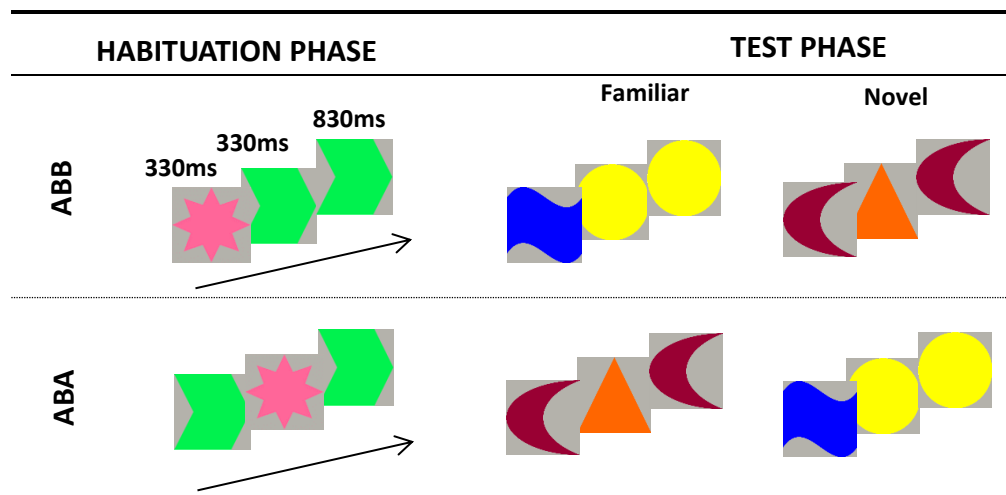


Figure 3.1 Schematic representation of stimuli and procedure used in the infants’ RL task.

Language measures

At 24 months of age, infants’ language abilities were measured through the parent-administered questionnaire ‘Primo Vocabolario del Bambino (PVB), Parole e Frasi’ (Caselli & Casadio, 1995), which is the Italian version of the ‘MacArthur-Bates Communicative Development Inventories (CDI): Word and Sentences’ Fenson et al., 1993). Parents filled in the questionnaire online via Survey Monkey. The PVB provides measures of expressive vocabulary and early grammar abilities in toddlers aged 16-30 months. Expressive vocabulary is quantified as the number of words marked by parents in a list of 670 words as

being actually produced by the child (Vocabulary). Grammar abilities are quantified as the mean number of words included in three utterances provided by the parents as examples of the longest utterances that the child produces (Mean Length of Utterance, MLU). Hence, higher Vocabulary scores and MLU scores indicate, respectively, higher expressive vocabulary and higher grammar abilities.

Analytic strategy

Three sets of statistical analyses were conducted. Firstly, because our sample did not match exactly with that tested by Bulf et al. (2017), we performed two Analyses of Variance (ANOVAs) on infants' looking times during the habituation and test phase of the RL task to determine whether, as a group, infants were able to perform the task. Secondly, to investigate the relation between infants' RL skills at 7 months of age and their linguistic abilities at 24 months, we conducted correlation analyses between infants' performance at discriminating between novel and familiar test trials during the RL task and their Vocabulary and MLU scores at the PVB. Thirdly, to further test the predictive role of visual RL on language outcome, we conducted a path analysis, which is commonly used to examine relationships among variables and test theoretical causal models when multiple variables are involved. Accordingly, we included discrimination performance in the RL task as the independent variable and Vocabulary and MLU scores as dependent variables.

Results

Rule learning abilities at 7 months

All infants reached the habituation criterion with a mean of 8.41 (SD = 3.12) trials and a mean looking time of 94 seconds (s) (SD = 50.22). An ANOVA with habituation rule (ABB vs. ABA) as the between-participants factor and habituation trials (first three vs. last three) as the within-participants factor confirmed the presence of an overall significant decline in infants' mean looking times from the first three (M = 50.02 s, SD = 5.17) to the last three habituation trials (M = 19.52 s, SD = 2.13), $F(1,25) = 78.98$, $p < .001$, $\eta^2 = .760$, which was not modulated by the rule embedded in the habituation sequences ($p_s > .3$). No differences in overall looking time or number of trials to habituate were found across the two habituation conditions (both $p_s > .3$).

To determine whether infants were able to discriminate between the familiar and the novel sequences at test, a repeated-measure ANOVA was performed on total looking times

during test trials with habituation rule (ABB vs. ABA) and test order (familiar first vs. novel first) as between-participants factors, and test trial pair (first vs. second vs. third) and test trial type (novel vs. familiar) as within-participants factors. The analysis revealed a main effect of test trial type, $F(1,23) = 12.12$, $p = .002$, $\eta^2 = .345$, whereby infants looked significantly longer to the novel test sequences ($M = 9.29$ s; $SD = 1.17$) than to the familiar ones ($M = 6.52$ s; $SD = .92$) (Figure 2). There was also a main effect of test trial pair, $F(2,22) = 9.15$, $p < .001$, $\eta^2 = .51$, revealing a decrease in infants' overall looking times from the first ($M = 10.02$ s, $SD = 1.34$) to both the second ($M = 7.24$ s, $SD = 1.09$; $p = .011$) and the third ($M = 6.46$ s, $SD = .80$; $p < .001$) trial pairs. No other effects or interactions were significant (all $ps > .1$).

These results indicate that infants were capable of abstract RL, as they extracted and learnt the ABB and the ABA rules instantiated over visual sequences of artificial geometrical shapes, and generalized them to novel shapes that had no surface features in common with those on which learning took place.

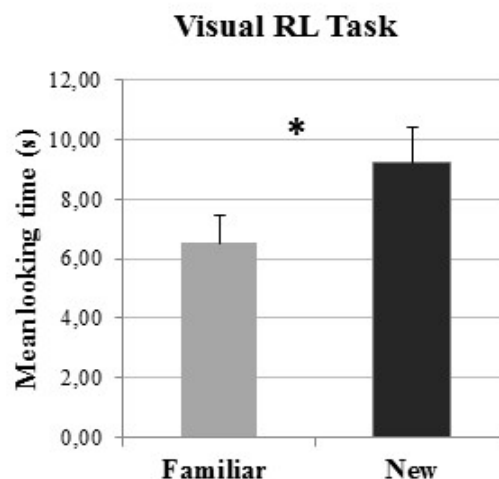


Figure 3.2 Mean looking time to the novel and familiar test sequences during test phase of the visual RL task. *: $p < .005$.

Correlation and path analysis between infants' RL abilities and later language outcome

To explore the relation between RL abilities and linguistic outcomes we correlated infants' discrimination performance between novel and familiar test trials in the RL task at 7 months with their syntactic and lexical abilities at 24 months, as assessed through the PVB questionnaire (MacArthur, CDI). To obtain a measure of infants' discrimination performance in the RL task, a novelty preference score was computed for each infant by subtracting the

total looking time towards familiar test trials from the total looking time towards novel test trials. Measures of syntactic and lexical abilities were obtained by assessing, respectively, the mean length of utterances, i.e. MLU ($M = 3.82$, $SD = 2.76$), and the number of words produced, i.e. Vocabulary ($M = 249.64$, $SD = 158.73$), as reported by the parents through the PVB questionnaire. Because not all of the parents filled out the PVB questionnaire in its entirety, the correlation analyses on syntactic and lexical abilities were conducted on different number of infants. Specifically, the correlation between the novelty preference score and the Vocabulary measures of lexical abilities was conducted for only a subset of the sample (25 infants, age range = 24 months - 24 months and 18 days, $M = 24$ months and 8 days). Despite the fact that Vocabulary and MLU measures were significantly correlated one with the other (Pearson $r(22) = .78$; $p < .001$), novelty preference score was not significantly correlated with Vocabulary (Pearson $r(22) = .16$, $p = .433$) but was positively correlated with MLU (Pearson $r(25) = .39$, $p < .005$) (Figure 3.3).

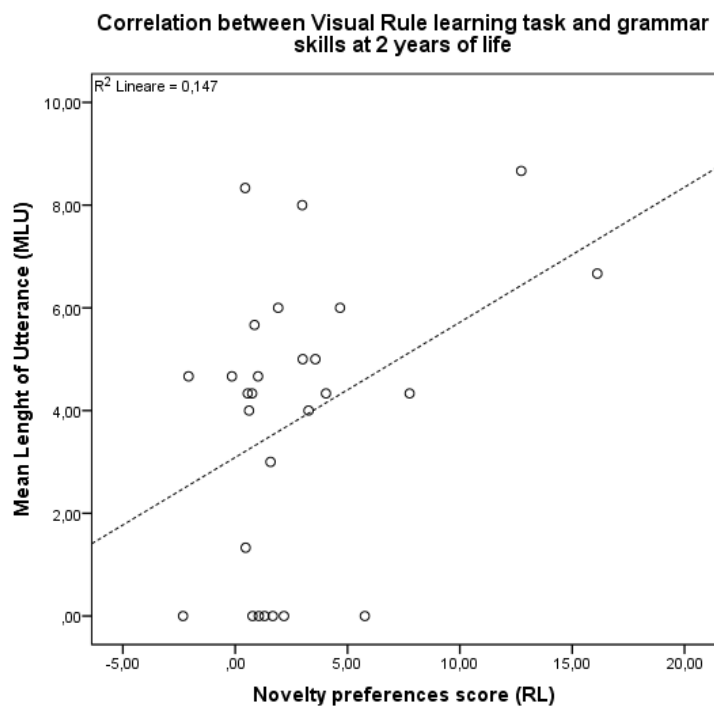


Figure 3.3 Correlation between infants' performance in the RL task and their syntactic ability at 2 years of age (MLU, mean length of utterances).

In order to further evaluate the specificity of the predictive relation between performance in the RL task and grammar skills at 24 months, we performed a path analysis considering novelty preference score as the independent variable upon MLU and Vocabulary, which were

both entered as dependent variables. The path analysis was performed through M-PLUS software version 7 (Muthén & Muthén, 2014), which simultaneously models all paths, giving more powerful, accurate and robust estimation of the effects. The model provided a good fit to the data, $X^2(3) = 29.36$, $p < .001$; RMSEA = .000, CI (90%) = .000 - .000; CIF = 1.00, SRMR = .000. Standardized estimates of path coefficients are depicted in Figure 3.4. The regression model showed that infants' novelty preference scores in the RL task explained 15% of the variance of the MLU outcomes, accounting for a link between early RL ability and later developing grammatical skills. Of note, novelty preference scores did not predict Vocabulary outcomes, Beta = .16; $p > .382$, indicating that early RL abilities specifically predicts later grammatical aspects of linguistic competences.

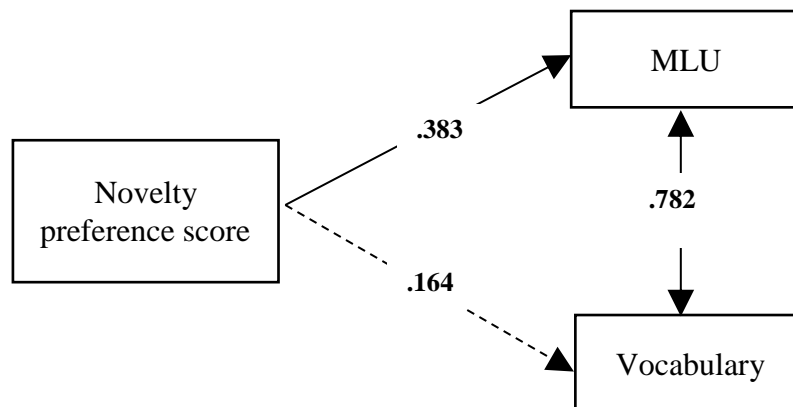


Figure 3.4 Regression model showed that infants RL ability (novelty preference score) predicts their grammatical abilities (MLU) but not their lexical abilities (Vocabulary) at 24 months of age.

Discussion

RL is a mechanism present in the first year of life and refers to the ability to detect high-order rules (ABB/ABA/AAB) from sequences of elements and generalize them to novel stimuli (Marcus et al., 1999). It has been shown that RL operates with either linguistic stimuli (e.g., Frank, et al., 2009; Marcus et al., 2007; Marcus, et al., 1999), and visual stimuli (e.g., Bulf et al., 2017; Johnson et al., 2009; Saffran et al., 2007), revealing a domain-general nature. Even though it has been proposed that preverbal infants' RL is related to the acquisition of grammatical skills in the first year of life (Marcus et al., 1999), no studies have investigated the presence of a direct link between early RL ability and later linguistic development.

The presents study was aimed to investigate whether visual RL in 7-months-old infants might predict their grammar development at 2 years of life. A group of infants,

partially composed by the sub-group sampled in Bulf et al.'s (2017) study was followed longitudinally, measuring their linguistic (vocabulary and grammatical) skills at 24 months of life. We first analysed visual RL ability in this sub-group, assessing whether infants were able to extract and generalize ABB or ABA high-order rules from a sequence of geometric shapes. After being habituated to an ABB or an ABA rule, they were tested with both an ABB and an ABA sequence. Results showed that infants were able to discriminate between novel and familiar rules during the test phase, providing evidence that they extracted and generalized the habituation rule. The link between infants' RL ability at 7 months of age and their later language development was measured correlating infants' performance at 7 months of age with their linguistic outcome. Our findings showed a linear relationship between the ability to discriminate visual rules and later grammatical ability: infants who were better in discriminating between new and familiar sequences, irrespective of the rule complexity, had a higher MLU. Additionally, the regression model revealed that infants' RL ability explained 15% of the variance of the MLU outcome but did not predict the vocabulary outcome, even though a correlation between grammar and vocabulary outcome was founded. This result shows that visual RL ability in early infancy is related to later grammatical outcome, but not to the vocabulary outcome. While the link between infants' RL ability and the grammatical outcome has been proposed by several studies (Endress and Bonatti, 2016; Marcus, 2000; Marcus et al., 1999; Peña et al., 2002), this is the first empirical evidence about the presence of this link in a study in which a group of infants was followed longitudinally from early to late infancy.

These data are in line with earlier findings that suggest that vocabulary comprehension and production is more related to infants' visual statistical learning mechanisms (Ellis et al., 2014; Shafto et al., 2012). It is still not clear whether SL and RL play a different role in the development of linguistic skills, or whether they are part of a same mechanism in which both statistics and high-order rules depend on the relevance of the pattern of distributional information (Aslin and Newport, 2014; Perruchet and Pacton, 2006). Irrespective of this debate, our study, along with previous findings on visual sequences learning (Ellis et al., 2014; Shafto, et al., 2012), suggests that learning merely contingencies between elements (SL) is more related to lexical development, whereas extracting high-order rules (RL) is more related to the development of grammatical skills (Endress and Bonatti, 2016; Marcus, 2000; Marcus et al., 1999; Peña et al., 2002). Indeed, learning the grammar structure embedded in the utterances requires the ability to keep track of the relative position of the words in the sentence (Mintz, et al., 2002; Mintz 2002, 2003) and to categorize and generalize this

information to novel linguistic elements, an ability that resembles rule learning instead of statistical learning mechanisms.

Results from the present study demonstrate that an early implicit learning and domain general mechanism (visual RL) predicts individual differences in the development of language skills. Of course, while the CDI questionnaire we used to measure infants' linguistic outcome at 2 years of age (Fenson et al., 1993) is reported to be a validate measure with a high reliability, and the mean length of utterances (MLU) is considered to accurately predict the grammatical ability specifically when it is used before three years of life (Devescovi and Pizzuto, 1995). However, MLU does not provide information about the qualitative aspect of the language acquisition such as which syntactic structures are used by children (Klee and Fitzgerald, 1985). It would be interesting to follow infants until 36 months of life and to utilize a measure based on a qualitative analysis of grammatical outcome, such as the use of morphemes, in order to gain more information about which specific aspect of grammar skills are related with the ability to extract and generalize adjacent and not adjacent repetition patterns.

The present study also suggests the possibility to use visual RL task as a tool in studying the developmental trajectory of infants at risks for language impairments and dyslexia. Indeed, a deficit in extracting and generalizing high-order rules might compromise the future development of grammatical skills. While evidence has been provided regards deficits in extracting the statistical information within linguistic sequences in children diagnosed for language impairment (Evans et al., 2009) and in infants at risk for dyslexia (Kerkhoff et al., 2013), no studies have investigated whether RL might be a marker task for the development of language disabilities. In addition, our findings suggest that the link between early implicit learning impairments and atypical language development might be assessed using visual sequences. This might disentangle whether language impairments lie on language-specific or domain-general implicit learning deficits.

CHAPTER 4

VISUAL RULE LEARNING IN CHILDREN WITH THE FULL-BLOWN DIAGNOSIS OF DEVELOPMENTAL DYSLEXIA

This chapter will be focused on the functioning of visual rule learning (RL) in children with a diagnosis of developmental dyslexia (DD). As discussed in chapter 1, the declarative/procedural model (Ullman, 2004) proposed that an impairment in implicit learning mechanisms might explain the wide-range of deficits reported in language, reading and social disorders. On this account, a growing number of studies have started to investigate the functioning of implicit learning mechanisms in individuals with a diagnosis of SLI, DD and ASD to better understand at what level these mechanisms are impaired in these populations (Nicolson and Fawcett, 2007; Ullman, 2004,2016). However, given the heterogeneity of these disorders it became critical to investigate the specific sub-components of implicit learning abilities to better understand the type of impairment underlying language or reading skills (e.g., Gabay et al., 2015; Mainela-Arnolds and Evans, 2014; Sigurdardottir, Danielsdottir, Gudmundsdottir, Hjartarson, Thorarinsdottir, et. al 2017).

Capitalizing on these evidences, the aim of the study reported in this chapter is to investigate whether visual RL abilities are affected in 8- to 10-years-old children with DD comparing their performance with a group of typically developing (TD) children, and whether this ability is related with children's language and reading skills. This project is still ongoing in collaboration with the IRCCS 'E. Medea' (Bosisio Parini, Lecco). A further aim of the project is to investigate the functioning of visual RL in 5-years-old children with a diagnosis of SLI in order to further investigate the divergence and similarity between these two disorders (Ramus et al., 2013).

Introduction

Developmental Dyslexia (DD) is defined as a specific and persistent difficulty in learning to read accurately and fluently despite average intelligence and adequate education and socio-cultural opportunities, and in the absence of sensory deficit in visual and auditory modalities (APA, 2013). In literature, there is a widespread agreement that the difficulty in recognizing written words in DD is related to a phonological deficit. Indeed, learning to read involves the mapping between letters and mental representation of their sound (Ramus et al., 2003; Snowling, 2001). However, other aspects of linguistic skills are often impaired in DD, as difficulties in comprehension and production of complex syntactic constructions (Bar Shalom, Crain and Shankweiler, 1993, Robertson and Joanisse, 2010), in morphology (Joanisse, Manis, Keating, and Seidenberg, 2000) and in morpho-syntactic skills (Cantiani et al., 2013a; Cantiani et al., 2013b; Guasti et al., 2015). Some of the deficits that characterized the linguistic production and comprehension in DD appear similar to those seen in individual with SLI (Bishop, 2002; Bishop and Snowling, 2004), and, in most cases, comorbidity and overlap between DD and SLI is reported (Bishop and Snowling, 2004). These evidences further strengthen the hypothesis that the clinical profile of DD is characterized by different deficits in multiple dimensions, as grammatical and phonological skills, rather than by a specific deficit in the decoding of written word (Ramus et al., 2013).

In addition to the phonological hypothesis (Ramus et al., 2003; Snowling, 2001), the declarative/procedural model posits that an impairment in implicit learning mechanisms might underlie the motor, phonological and language difficulties that characterized DD (Ullman, 2004). This model was further confirmed by a recent meta-analysis that revealed that individuals with DD had, on average, worse procedural learning abilities than non-diagnosed individuals (Lum, Ullman, and Conti-Ramsden, 2013). More recently, researchers have started to focus on aspects of DD implicit learning abilities more related to auditory and visual sequential learning, i.e. on learning mechanism that allows to acquire regularities in a sequence of elements. The investigation of the role of sequential learning mechanisms in DD has provided mixed results (for a review see Schmalz, Altoè, and Mulatti, 2017). For example, Nigro, Jiménez-Fernández, Simpson, and Defior (2016), tested the ability to implicitly acquire positional regularities from unfamiliar visual stimuli in children with diagnosis of DD and typically developing (TD) children. Children were exposed to a visual string of shapes presented in specific positions, i.e. S₁, S₂, S₃, S₄. During the test phase, participants were asked to identify ‘legal see’, ‘legal unseen’, and ‘illegal’ strings. The ‘Legal

see' sequences were composed by the same string seen during exposure phase, the 'legal unseen' sequences contained new stimuli that followed the same patterns of learning sequence, and the 'illegal' sequences were characterized by new stimuli embedded in new patterns (e.g., S₃, S₂, S₁, S₄). Results did not reveal any difference between TD and DD children, suggesting that sequential learning abilities were not impaired in DD children. On the contrary, Pavlidou and Williams (2014) found an impairment in sequential learning in children with DD. Children were familiarized with visual sequence of shapes that contained rule-like patterns with different levels of complexity. During test, children were requested to recognize from a new set of stimuli which sequences followed the pattern presented during the familiarization phase. Results showed that the TD group was able to acquire the rules, whereas children with DD exhibited difficulties in learning this type of information. Even though the investigations of sequential learning mechanism in DD report mixed results, there is a widespread agreement about the hypothesis of a general implicit learning impairment (both in the linguistic and in the visual domain) in individuals with DD (Folia, Uddén, Forkstam, Ingvar, Hagoort, and Petersson, 2008; Lum et al., 2013; Nigro et al., 2015; Pavlidou and Williams, 2014).

It is worth noting that some of the tasks used to investigate the role of sequential learning in DD involved both statistical information and high-order rule abstraction, requiring participants to recognize complex statistical relationships between elements and to apply the resulting knowledge to new elements (Kahta and Schiff, 2016; Pothos, 2007). However, as already reported in the chapter 1 of the present thesis, statistical learning (SL) and rule learning (RL) operate on the environmental input in different ways. More specifically, SL allows to learn regularity based on statistical relationships – transitional probabilities - across elements (Saffran et al., 1996), whereas, RL allows to extract high order rules from a sequence of elements and to generalize them to novel stimuli (Marcus et al., 1999). Moreover, studies carried out with adults from the general population suggested that SL and RL are linked to different aspects of language processing, as SL seems to be related to phonological skills and, more specifically, to the ability to learn the grapheme-phoneme correspondences (Aricoli and Simpson, 2012), while RL appear related to syntactic skills (Endress and Bonatti, 2007; Marcus, 2000, Marcus et al., 1999; Peña et al., 2002; see also the study reported in chapter 3).

A recent study by Gabay and colleagues (2015) investigated the specific ability to track statistical relationships from speech and not speech (musical tone) elements in adults with and without DD. For the speech condition, participants were exposed for 2 minutes to a

continuous speech stream consisting of four three-syllable nonsense words (i.e., *tupiro*, *golabu*, *bidaku*, *padoti*) repeated in random order, in which the transitional probability between the syllables within the same word was higher (1.0) than the transitional probability across words. After the learning phase, participants performed a force-choice task in which words (syllables with a high transitional probability) and part-words (syllables with a low transitional probability) were presented. Participants were asked to judge which of the two stimuli, i.e. word vs. part-word, were more familiar to the stimuli previously heard during the familiarization phase. The same procedure was used with musical tones. Results showed that individuals with DD were less accurate in extracting the transitional probabilities embedded in the auditory sequences for both speech and not speech materials than individuals from the control group. Moreover, a positive link between individuals' SL ability and their reading skills was found. The same pattern of results was obtained when SL in DD was investigated using visual stimuli (i.e., sequences of geometrical shapes), as participants with DD performed more poorly on visual statistical learning tasks than the control group (Sigurdardottir et al., 2017). Overall, these evidences reveal an impairment in individual with DD in extracting statistical relationships from both auditory and visual sequences (Gabay et al., 2015; Nicolson and Fawcett, 2011). While several studies have investigated the functioning of SL in DD, to our knowledge no studies have instead assessed the role of RL mechanisms in DD. As it has been proposed that DD is also characterized by morpho-syntactic and syntactic impairments (Cantiani et al., 2013a; Cantiani et al., 2013b; Guasti et al., 2015) and that RL is related to the extraction of the grammatical structures (Endress and Bonatti, 2007; Marcus, 2000; Marcus, et al., 1999), the study of RL in DD is crucial in order to better understand whether and how implicit learning accounts for the emergence of this disorder.

In order to fill the gap in literature, the present study was aimed at investigating the functioning of visual RL in DD. To this end, visual RL ability in a group of 8-11-years-old children with DD were compared with a control group of TD children. Children were exposed to a sequence of triplets of visual shapes organized into ABB and ABA patterns, and subsequently tested for their ability to detect the rule to which they have been exposed during the learning phase. We used visual shapes to dissociate RL abilities from the process of linguistic materials, and to investigate the presence of a domain-general impairment in RL mechanism, as hypothesized by the procedural/declarative model (Nicolson and Fawcett, 2011; Ullman, 2004). We expected that children with DD would show difficulties (less

accuracy and higher response times) to extract and generalize abstract rules respect to the TD control group.

Moreover, children's visual RL abilities were correlated with their linguistic and reading skills. Linguistic skills were assessed respectively by a syntax comprehension test ('Battery for the evaluation of language in children aged 4-12 years'; Marini, Marotta, Bulgheroni, and Fabbro, 2015) and by a morphological manipulations test called 'Co.Si.Mo'¹ ('Competenze sintattiche e Morfosintattiche – Syntactic and Morphosyntactic skills', Milani et al., 2005). Reading skills were assessed through word and non-word reading test ('Battery for the Assessment of Developmental Dyslexia and Dysorthographia-2', DDE-2, Sartori and Job, 2007) that measures lexical and sub-lexical reading routes (e.g., Coltheart, Rastle, Perry, Langdon, and Ziegler, 2001), and through fluency in reading a text test ('MT Reading Tasks', Cornoldi and Colpo, 1998). We expected a correlation between visual RL and syntactic skills, as suggested by the hypothesis that RL is involved in grammar acquisition (Endress and Bonatti, 2007; Marcus, 2000; Marcus, et al., 1999) and by the empirical evidence of a link between RL ability and grammar outcome in infancy (chapter 3). Moreover, we expected a correlation between visual RL and the general proficiency in reading a text, as text reading is a complex cognitive process that involves the integration of an adequate knowledge of the rules governing lower-level processing and the automatization of word-level decoding operations (Kim, 2017).

Methods

Participants

Thirty-one 8-11-years-old children with a diagnosis of Developmental Dyslexia (DD) and 27 typically developing children (TD) participated in this study. All children with DD had been referred to the Unit of Cognitive Psychology and Neuropsychology of the IRCCS Eugenio Medea (Bosisio Parini, Lecco), while children of the TD group were recruited from a local school ('Istituto Comprensivo de Amicis', Treviglio). All participants voluntarily took part in the study after parents had given their informed consent. The study had been approved by the Ethics Committee of the IRCCS Eugenio Medea, according to standards of the Helsinki Declaration (World Medical Association, 2013).

All participants were native speakers of Italian. Children were included in the study if they had an intelligence score within the normal range on a standardized intelligences test (IQ

¹ Co.Si.Mo is an unpublished battery with consistent normative data for children aged 8-14 years-old battery

>25 percentile; assessed by 'Raven's Coloured Matrices' test; Raven, 2000). All participants with DD had received a clinical diagnosis of DD based on standard inclusion and exclusion criteria (DSM-V, American Psychiatric Association 2013). Co-morbidity with attention deficit hyperactivity disorder (ADHD) or other psychopathological conditions were excluded. In addition, in order to be included in the study, children with DD should currently have a performance in reading speed and accuracy two (or more) SDs below the mean in at least one of the age-standardized Italian reading tests included in the battery (word, non-word, and text reading). On the contrary, in order to be included in the TD group, children had to obtain a score within the normal range (> -1 SD) on all tests included in the battery assessing reading and language skills.

Overall, from the DD group two children were excluded because they had comorbidity with ADHD; seven children were excluded because they obtained a score above -2 SD in reading and language tests; and four additionally children were excluded because their total accuracy in the RL task was more than 2.5 SD below the overall average of the group (this was the same criteria used in Bertels, Boursain, Destrebecqz, and Gaillard, 2015). From the TD group, four children were excluded because they obtained a score below -1 SD in reading and language tests; four additionally children were discarded from the analysis because their total accuracy in the task was below 2.5 SD (same criteria used for DD group). The final samples were composed by 18 children (8 females) with diagnosis of DD and with a mean age of 9.22 years ($SD= 0.77$), and by 19 TD children (11 females) with a mean age of 9.32 years ($SD= 1.07$).

Participant characteristics compared with a series of t-tests are shown in Table 4.1. Reflecting the recruitment criteria, the DD group differed significantly from the TD group in all reading scores. In addition, group differences emerged in the Co.Si.Mo test, evaluating morpho-syntactic skills.

	TD (n=19)	DD (n=18)	t tests		
	Mean (SD)	Mean (SD)	t (35)	<i>P</i>	Cohen's d
IQ	103.37 (10.83)	104.18 (8.44)	- 0.25	.802	-0.08
MT text speed	0.38 (0.52)	-1.30 (0.78)	7.76	<.001	2,62
MT text accuracy	0.30 (0.33)	-1.90 (1.56)	5.87	<.001	1.98
WR speed	0.55 (0.68)	-2.84 (3.52)	4.02	.001	1.36
WR accuracy	0.47 (0.51)	-2.90 (2.65)	5.17	<.001	1.75
NW speed	0.57 (0.69)	-1.83 (1.72)	5.51	<.001	1.86
NW accuracy	0.53 (0.49)	-1.55 (1.59)	5.33	<.001	1.80
Co.Si.Mo	0.58 (0.55)	-0.62 (1.27)	3.70	.001	1.25
Syntactic Comprehension	0.39 (0.61)	0.20 (0.62)	0.96	.344	0.32

Table 4.1 Participants characteristics that reflected the recruitment criteria. The two groups differed significantly (in bold) in all reading scores and in the subtest of the Co.Si.Mo battery that evaluated the morpho-syntactic skills.

Successively, to further investigate the relationship between RL mechanism and reading and linguistic skills, the participants prior excluded because of reading scores (n = 7 from the group of children with DD and n = 4 from the group of typically developing children) were added to the sample, resulting in a total sample of 48 children.

Test Material and Procedure

The experiment took place in a quiet and well-light room. For each participant, the session lasted about one hour and comprised the assessment of general cognitive ability, language and learning skills and the visual rule learning task.

General cognitive measures

The general cognitive ability was assessed through a computer version of the non-verbal intelligence scale ‘Raven’s Coloured Matrices’ (CPM, Raven, 2000). This test is designed for children aged 5–12 years, elderly individuals and mentally or physically impaired individuals (norms for children are available). The CPM consists in three sets of visual matrices (A, Ab and B) with increasing difficulty. Each set is composed by 12 visual matrices in which a series of patterns with missing parts are presented. The participants were requested to select the best-matched figure as the missing part from 6 alternatives depending on the given pattern in each item. The Raven’s CPM produces a single raw score corresponding to the total number of matrices completed correctly (maximum score = 36). This score can be converted to a percentile based on normative data collected from various groups. Here, a QI score has been calculated in percentile value (Italian version: ‘Progressive Matrici Colore, serie A, Ab,

B'; Raven, J.C., 1947) and transformed in standardize score ($M = 100$; $SD \pm 15$; see Table 4.1).

Reading ability assessment

Reading ability was assessed through two different tasks.

Word and non-word reading was assessed with two subtests from an Italian standardized battery ('Battery for the Assessment of Developmental Dyslexia and Dysorthographia-2', DDE-2; Sartori and Job, 2007). Speed and accuracy z-scores were computed for single word (4 lists of 28 words) and non-word reading (3 lists of 16 non-words).

Text reading was assessed with widely used Italian tests ('MT Reading Tasks', Cornoldi and Colpo, 1998) providing accuracy and speed scores in reading aloud age-normed texts (z-scores were computed).

Language ability assessment

Language ability was assessed through two different tasks.

Syntactic comprehension was assessed with sub-test 10 of the 'Battery for the evaluation of language in children aged 4-12 years' (Marini et al., 2015). Italian norms are available for children aged 4-12 years. Forty sentences of increasing syntactic complexity were auditorily presented, and children were asked to match each sentence with one out of four pictures (one target and three distractors). Referring to the norms, z-scores were computed.

Morphological skills were assessed with a subtest of the battery 'Co.Si.Mo' (Competenze sintattiche e Morfosintattiche – Syntactic and Morphosyntactic skills, Milani et al., 2005), with unpublished but with consistent normative data for children aged 8-14 years-old. In this task, children were both auditorily and visually presented with non-words. The production of different morphological manipulations of non-words was requested. Specifically, manipulations of noun-like non-words (e.g., *prico*) involved the creation of plural, diminutive or augmentative forms, whereas manipulations of verb-like non-words (e.g., *sencare*) involved the creation of infinitive, substantive, gerundive or conditional forms. One point was assigned for each correct answer, while 0.5 points were assigned for other neologisms correctly formulated. Overall, the subtest included 22 manipulations.

Visual Rule Learning Task (VRL)

Twelve coloured shapes were presented as stimuli on a grey background. The shapes were shown on a 15-inch computer monitor with a resolution of 1280x800 and were embedded in a virtual square of $10^\circ \times 10^\circ$ visual angle. The shapes were organized in triplets following an

ABB (repetition of the same element B in the last position) or an ABA (not adjacent repetition of the A element) patterns.

The task was run with the software E-Prime 2.0 on a Toshiba Intel Core 2 vPro laptop. Before the presentation of the experimental trials, a training phase composed by a minimum of three to a maximum of six trials was administered to be sure that children had understood the task. Children had to provide two consecutive correct responses in order to start the experimental tasks. The experimental task that was composed by 64 trials and each trial was divided in a learning and in a test phase (Figure 4.1). During the learning phase, children were presented with 3 triplets of shapes organized into either an ABB or an ABA rule. Each triplet was shown one at a time following a sequential presentation from left to right. The first shape was displayed on the left side of the screen for 330 milliseconds, the second was shown in the middle of the screen for 330 milliseconds, and the last shape was presented on the right side of the monitor for 830 milliseconds. Each triplet was separated from the following one by a blank of 500 milliseconds (ms), and each learning phase lasted 4.5 seconds. To mark the beginning of the test phase, a blue screen with a cross in the middle was showed for 500 ms. In the test phase a new triplet of shapes was presented following the ABB or ABA rules. After the test triplet, a green and a red smiling face with a diameter of 5 cm (5°) were presented on the left side and on the right side of the screen until the participant's response. Participants were asked to respond whether the order of presentation of the shapes seen during the test phase was the same order in which shapes were presented during the learning phase or not. Participants had to press one of two buttons on the keyboard corresponding to the green smiling face (congruent response) or the red smiling face (incongruent response). The order of response keys (congruent left, incongruent right side or vice versa) was randomized between participants. In order to investigate whether children were able to generalize the rule presented during the learning phase, eight unique shapes were presented during the learning phase, and four new shapes were presented during the test phase. For the learning phase, four shapes were assigned to A group and four to B group, randomly combined by the software into ABB and ABA patterns. For the test phase four novel shapes were presented, two shapes belong to A group and two to B group.

Manual response times and accuracy were measured as dependent variables.

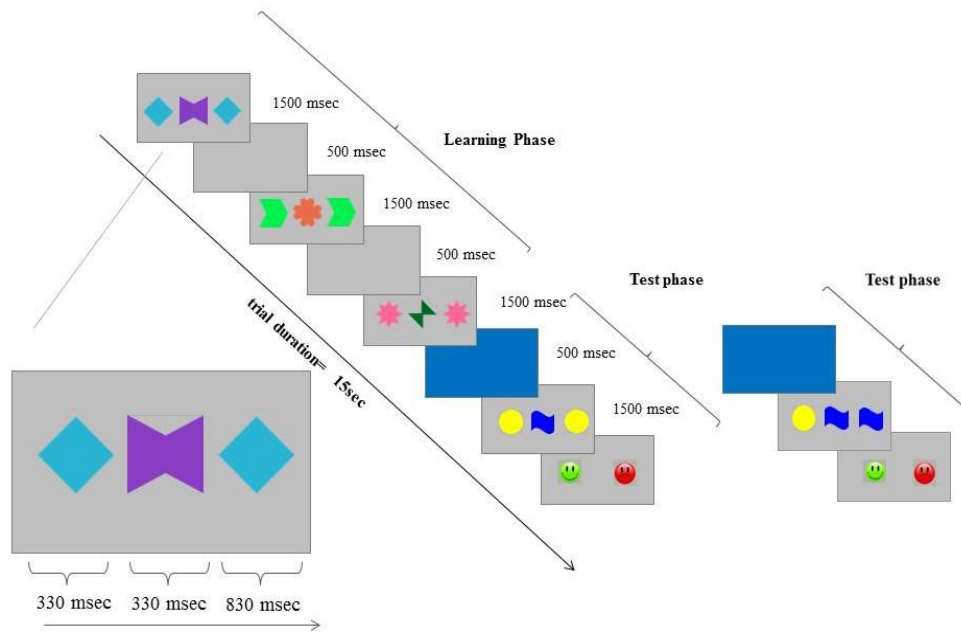


Figure 4.1 Schematic representation of the stimuli and procedure used in the visual RL task.

Statistics Analysis

First, in order to investigate group differences in extracting and generalizing rules, two repeated-measure ANOVAs were performed separately on the accuracy (d') and response times (RTs) obtained in the visual rule learning task. Accuracy was investigated through the d' index, that was calculated from hit and false alarm rates for each participant (e.g., Stanislaus and Todorov, 1999). The d' index is particularly appropriate in tasks where a yes/no response is requested. It allows to estimate the accuracy in detecting the congruent or incongruent stimuli by removing the effect of high/low conservative criterion adopted by individual participant to respond (for more explanations about the methodology see: Stanislaus and Todorov, 1999). A value of 0 indicates an inability to distinguish between congruent or incongruent conditions; a positive value indicates good performances and a negative value can indicate response confusion (i.e. responding 'yes' when intending to respond 'no', and vice versa). The ANOVA on the d' index was performed with one between-participant factor (Group: TD vs. DD) and only one within-participant factor (Rule of learning phase: ABB vs. ABA). The ANOVA for RTs was conducted with one between-participant factor (Group: TD vs. DD) and two within-participant factors (Rule of learning phase: ABB vs. ABA; and Congruency: congruent vs. incongruent condition).

Successively, to further explore the overall relationship between the individual ability to detect and generalize patterns and reading/language skills (irrespective from the diagnostic category), Pearson correlations were computed between the standardized scores obtained during the neuropsychological evaluation (general cognitive ability, reading and language skills) and total d' index and total RTs, estimated as the average across different experimental task conditions. As already mentioned in the participant section, for this set of correlational analysis the criteria to be included had been extended. Specifically, some of the participants that were excluded for the group comparison analysis because they did not reach the restricted criteria in the neuropsychological assessment to be part of DD or TD group were included in the correlational analyses. For the correlational approach, increasing sample size allowed us to increase variability and to better understand individual differences, given the great heterogeneity in reading and language skills that characterized both individuals with typical development and with diagnosis of DD (Castles and Coltheart, 1993; Pennington, 2006, Ziegler, Castel, Pech-Georgel, George, Alario, and Perry, 2008).

Results

Group comparison

The ANOVA on the accuracy d' index revealed a main effect of group, $F(1,35) = 5.56$, $p = .040$, $\eta^2 = .115$. Overall, the TD group was more accurate ($M = 2.76$, $SD = 0.10$) than the DD group ($M = 2.45$, $SD = 0.11$), as reported in Figure 4.2. No other significant effect was found, $ps > .205$.

The ANOVA on RTs revealed a main effect of Congruency, $F(1,35) = 9.12$, $p = .005$, $\eta^2 = .207$. RTs in the congruent condition were faster ($M = 745.33$, $SD = 39.81$) than those in the incongruent condition ($M = 817.74$, $SD = 46.90$). Surprisingly, neither main effect of group, $F(1,35) = 0.13$, $p = .723$, $\eta^2 = .004$; nor main effect of rule, $F(1,35) = 2.02$, $p = .164$, $\eta^2 = .055$, or interaction between groups, rule and/or congruency ($ps > .268$) were significant. Therefore, children in the TD and DD groups were equally fast to perform the task (TD group: $M = 796.47$; $SD = 58.34$; DD group: $M = 766.60$, $SD = 59.93$).

Comparison between TD and DD Groups

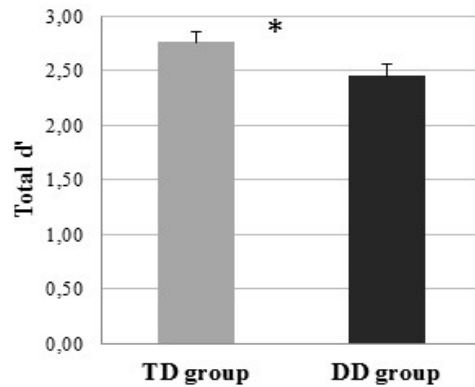


Figure 4.2 Mean d' index (+SE) for CNT and DD groups. *: $p < .005$.

Correlations

In order to further explore the relationship between the ability to extract and generalize abstract patterns and reading/language skills, we computed correlations analyses between the experimental task measures (d' index and RTs) and the scores obtained in reading and language on the entire sample of participants. These analyses were conducted to investigate the relationship between RL ability and individual language and reading skills independently by the diagnosis criteria (Gabay et al, 2015). Since in the group comparison analyses no effect were found according to the ABB and ABA rule conditions (neither for d' analyses nor for RTs), the conditions were collapsed and the mean d' ($M = 2.89$, $SD = 0.82$) and response times ($M = 778.66$, $SD = 265.68$) were used as variables for the correlations analysis.

First, positive correlations between experimental task measures (d' index and RTs) and Age and IQ were found (Table 4.2).

	AGE		IQ	
	<i>r (gl)</i>	<i>p</i>	<i>r (gl)</i>	<i>P</i>
d' prime	.199 (48)	.176	.336 (48)	.020
RTs	-.346 (48)	.016	-.442 (48)	.003
MT text speed	.169 (47)	.256	-.063 (47)	.674
MT text accuracy	.125 (47)	.403	.160 (47)	.282
WR speed	-.236 (48)	.107	.022 (48)	.880
WR accuracy	-.209 (48)	.154	.002 (48)	.992
NW speed	-.332 (48)	.021	-.037 (48)	.804
NW accuracy	-.141 (48)	.340	-.088 (48)	.550
Co.Si.Mo	.168 (48)	.253	.146 (48)	.323
Syntactic Comprehension	.316 (48)	.029	.254 (48)	.082

Table 4.2. Correlations between Age and IQ with experimental task measures (d' prime and RTs) and scores of reading and language tests. In bold the significant correlations.

To remove the effect of these variables, partial correlations to control for Age and IQ were computed for both d' index and RTs and raw scores of reading and language tests.

The analysis revealed that the accuracy (total d' index) in detecting and generalizing rules correlated positively with text reading speed, ($r(42) = .346, p = .021$). Moreover, a marginal significant correlation was found between the d' index and Syntactic Comprehension ($r(42) = .266, p = .081$). These correlations suggest that children that were more accurate in detecting and generalizing rules were characterized by better text-reading skills (speed) and by better syntactic comprehension skill. The following scatterplots show the reported correlations (Figure 4.3). To concern RTs, no significant correlations were found ($p > .140$).

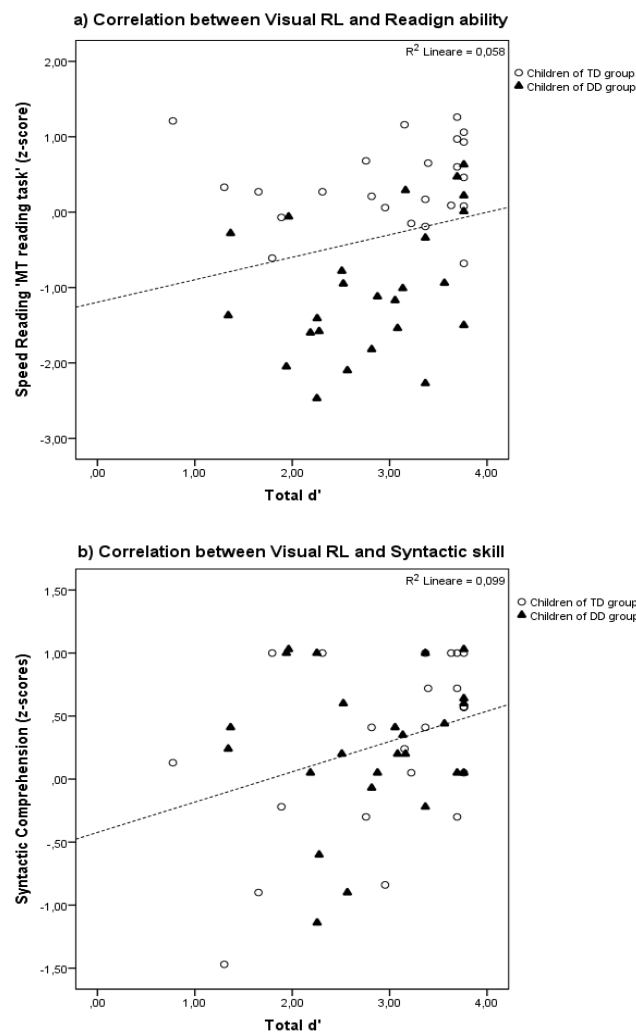


Figure 4.3 Scatterplots between total d' index in the visual rule learning task and (a) text-reading speed (on the bottom side, Cornoldi and Colpo, 1998) and (b) syntactic comprehension skills (on the up side, Marini et al., 2015).

In order to further explore the associations found between the accuracy at RL task and language and reading abilities, a set of correlations was computed for each group. The analysis revealed that in the TD group the d' index was positively correlated with syntax comprehension, $r(19) = .464, p = .034$, while in children with DD the d' index correlated with text reading speed $r(19) = .441, p = .046$.

Discussion

Rule learning (RL) is an implicit learning mechanism that allows to extract and generalize high order rules from a sequence of elements (Marcus et al., 1999). It has been proposed that this mechanism is crucial to extract the grammatical structure of language (Endress and Bonatti, 2016; Marcus et al., 1999; Peña et al., 2002), and the direct link between visual RL ability and the development of grammatical skill has been reported in the chapter 2 of the present thesis. Despite the relevance of RL in the acquisition of the grammatical structure of language and the presence of an impairment of grammatical skills in DD (Guasti et al., 2015), to the best of my knowledge no studies have investigated the functioning of RL in children with DD.

Starting from this lack, one of the aim of the present study was at investigating whether visual RL is impaired in children with a diagnosis of DD and whether it is related to reading and language skills. To this end, we compared 8-11-years-old children with DD and TD children in a visual RL task. After a brief exposure to simple rules containing adjacent and not adjacent repetitions (i.e., ABB and ABA), children were presented with a familiar and a novel rule (ABB or ABA) delivered by a new set of geometrical shapes, and were asked to identify the rule to which they were previously exposed. Linguistic and reading skills were assessed respectively by a syntax comprehension test (Marini, et al., 2015) and a morphological manipulations test ('Co.Si.Mo', Milani et al., 2005), and through a word and non-word reading test (Sartori and Job, 2007) and a fluency in reading a text test (Cornoldi and Colpo, 1998). Results showed that children from the DD and the TD groups were equally fast in identifying the rule during the test phase (TD group: $M = 796.47$ ms; $SD = 58.34$; DD group: $M = 766.60$ ms, $SD = 59.93$), and that the accuracy in identifying the rule was above the chance levels of 50% in both groups. However, the DD group was less accurate ($M = 89.44\%$, $SD = 5.96$) to detect and generalize the rule than control group ($M = 93.37\%$, $SD = 6.54$), suggesting that RL ability is intact in DD but less efficient than in TD children. This pattern of results is in line with previous studies that have found a less efficient implicit

learning abilities in DD using artificial grammar learning tasks (Pavlidou and Williams, 2014; Pavlidou, et al., 2010; 2009) and statistical learning tasks (Gabay et al., 2015; Sigurdardottir et al., 2017).

In order to examine the relationship between visual RL and linguistic and reading skills, we conducted a set of correlations on the entire sample. Results revealed that accuracy in identifying and generalizing visual rules was positively correlated with syntactic comprehension and speed in reading a text. This link between visual RL and syntactic comprehension confirms the relevance of visual RL mechanism in the acquisition of grammatical skills, in line with the study reported in chapter 2. In addition, when the correlations analyses were computed in the two groups separately, the RL ability appears to be related to grammar skill solely in TD group and not in DD group. This pattern of results suggests that the strategies used by DD children during a grammar comprehension task might involve skills that are different than those used by TD children. This interpretation is further supported by studies in children that measured ERP responses during a task that required a morphological manipulations , showing that DD probably used a lexical strategy rather than syntactic skills to perform the task, causing a specific drop in performance (Cantiani, Lorusso, Perego, Molteni, and Guasti, 2015; Cantiani et al., 2013a; Cantiani et al., 2013b). Unfortunately, our data do not enable to specify what type of mechanism may subserve the processing of grammar structures in DD population.

As the relationship between visual RL and the speed in reading a text found in the DD group, this evidence further confirms the existence of a relationship between reading skills and basic skills involving the processing of sequence information in DD (Jimenez-Fernandez, Vaquero, Jimenez and Defior, 2010). RL might be linked to complex aspects of reading process that are not confined to the lexical access or the grapheme-phoneme decoding. Indeed, the measure of lexical access (that we assessed by a word reading test; Sartori and Job, 2007) and grapheme-phoneme decoding (that we assessed by a non-word reading test; Sartori and Job, 2007) did not correlate with children's performance in the visual RL task. Specifically, during text reading, a stable representation of the relationships across the elements in the sentence can act as additional cue in decoding of written words (Muter, Hulme, Snowling, and Stevenson, 2004). Therefore, a deficit in RL might cause a noisy representation, increasing the cognitive demands of word recognition that, in turn, have a consequence in reading fluency. Further evidences are necessarily to examine the role of RL mechanism in reading skills.

To note, our results showed a positive relationship between the speed of processing in the visual RL task and the non-verbal fluid intelligence (Raven, 2000), suggesting that other variables, such as more efficient cognitive abilities, are likely to impact the speed of processing of visual patterns. This latter evidence confirms the importance for further investigate individual differences in the functioning of implicit learning mechanisms both in DD and in the general population (Arciuli, 2017; Kaufman, DeYoung, Gray, Jiménez, Brown, and Mackintosh, 2010).

To my knowledge, the present study is the first attempt to investigate the functioning of visual RL in children with DD, comparing their performance with a TD control group, and assessing the link between visual RL and reading and linguistic skills. Even though the phonological impairment is the most accredited hypothesis to clarify the reading deficits in DD (Ramus et al., 2003; Snowling, 2001), the present results further account for the possibility that a general implicit learning impairment could explain the heterogeneity of manifestation of reading deficits in DD (Nicolson and Fawcett, 2011). Indeed, visual RL mechanisms in our DD group seem to be less efficient than those found in the TD group, as revealed by the difference in accuracy in identifying the rule between the two groups. We have also found that, while children with DD showed a disadvantage in visual RL abilities when compared to the control group, their performance in the visual RL task was above chance. It is worth noting, however, that the explicit nature of our task might have co-opted compensatory top-down strategies that, in turn, might have improved the ability to learn and generalize the high-order rules in the DD group (Ullman and Pullman, 2015). Considering that our task might be not sensitive enough to reveal strong difference between the DD and the TD group, future researches should explore more directly the role played by RL mechanisms in the DD population using implicit tasks, such as serial reaction time or ERPs measures, or by providing children with no explicit instructions. While the present study does not definitely determine the functioning of RL ability in children with DD, it contributes to our understanding of implicit learning deficits in children with DD, and highlights the need to deeply investigate the role of different implicit learning mechanisms in this population.

CHAPTER 5

VISUAL STATISTICAL LEARNING IN 7-MONTHS-OLD INFANTS AT LOW RISK TO DEVELOP AN AUTISM SPECTRUM DISORDER

The next two chapters are focused on the investigation of the early neuropsychological markers of social and communicative impairments, i.e., autism spectrum disorder (ASD), specific language impairment (SLI) and developmental dyslexia (DD). As said in the introduction, the presence of an overlap in language and behavioural deficits and comorbidity across these disorders suggest that SLI, DD and ASD might share one or more of cognitive deficits linked to language and communicative skills (Bishop, 2002; Tomblin, 2011).

In this chapter will present a study that investigated visual statistical learning (SL) ability in infants at (low) familial risk to develop ASD by virtue of having parents with sub-threshold high traits. In the next chapter, I will report a study that has investigated visual SL and rule learning (RL) abilities in infants at (high) familial risk for SLI and DD by virtue of having a first-degree relative with diagnosis of SLI and/or DD.

This chapter is adapted from:

Bettoni, R., Riva, V., Cantiani, C., Riboldi, E., Molteni, M., Macchi Cassia, V., and Bulf, H. (under submission) Dysfunctions in infants' statistical learning are related to subthreshold autistic social impairments in their parents.

Introduction

Statistical learning (SL) is an early cognitive ability that allows us to detect statistical regularities distributed among space and time (Saffran et al., 1996) and represents one of the multiple approaches for the study of the broader cognitive construct of implicit learning, defined as learning without awareness or cognitive effort (Arciuli, 2017; Reber, 1967; Seger, 1997, 1998). Implicit learning is involved in the acquisition of more complex abilities such as linguistic, communicative, and social skills (Romberg and Saffran, 2010; Alcock, 2006; Perruchet and Pacton 2006; Bishop, 2002). For example, in the social field, learning of temporal patterns that are predictive of events and routines is crucial to infer the intention of the others (Lieberman, 2000; Ruffman, 2012).

A growing number of researches has recently suggested that an impairment in implicit learning mechanisms might be involved in the development of autism spectrum disorders (ASD) (Frith, 1970a, 1970b; Klinger, Klinger, and Pohlig, 2007), a heterogeneous neurodevelopmental disorder characterized by a deficit in social and communicative skills (APA, 2013). Indeed, individuals with ASD show difficulties to learn from the others' behaviour only by exposure and to take advantage from implicitly coding of social cues to adapt their behaviour according to circumstances (for a review see: Foti, De Crescenzo, Vivanti, Menghini, and Vicari, 2015; Obeid et al., 2016).

Studies devoted at the investigation of SL in ASD have found mixed results. For example, using a forced choice task, Mayo and Eigsti (2012), investigated the ability of 7-13-years-old high-functioning children to track transitional probabilities across linguistic sequences. Children was familiarized for 21 minutes to a continue sequence of syllables in which syllables within a 'words' had higher transitional probabilities (100% of predictability) than syllables across 'words' (33% of predictability). The accuracy to recognize words and part-words was major than chance in the ASD group and in a group of typically developing (TD) children, suggesting that children with ASD had an intact SL ability. However, other fMRI (Scott-Van Zeeland et al. 2010) and ERPs (Jeste et al., 2015) studies showed that children with ASD did not learn statistical relationship compared to TD peers. Specifically, fMRI study revealed markedly different patterns of activation between high-functioning children with ASD and TD during learning of artificial grammars composed by trysyllabic 'words' (Scott-Van Zeeland et al., 2010). In line with this evidence, Jeste and colleagues (2015) reported that 2- to 6-years-old ASD children had a reduced electrophysiological response during a visual SL task compared to a TD group. Using an oddball visual SL

paradigm adapted from Kirkham et al. (2002), children was exposed to a string of pairs of visual elements, in which the first shape was followed by a predictable shape for 90% of the trials (expected trials), or it was followed by a deviant element for 10% of the trials (unexpected trials). The findings revealed that, differently from the TD group, the ASD group did not show a difference between expected and unexpected trials in N1 and P300 amplitudes components, suggesting that ASDs' ability to extract transitional probabilities from visual sequences is less efficient than in TD children (for more details see Chapter 1, paragraph 1.4).

Overall, evidence from these behavioural and neurophysiological studies suggest that a difference in performance between ASD and TD individuals can be showed only at a neurophysiological level, as behavioural data are not powerful enough to reveal the presence of the difference. Most probably, this discrepancy can be explain considering that individuals with ASD might present difficulties in SL task at an implicit level, that is easily mapped by neurophysiological measures. Conversely, when the SL task requires an explicit (behavioural) response, ASD individuals might employ cognitive strategies that masked their implicit learning deficit (Nuske, Vivanti, and Dissanayake, 2013; Vivanti and Hamilton 2014; Vivanti and Rogers, 2014; Ullman and Pullman, 2015).

Here, we investigated the functioning of visual SL in infants at risk for ASD as a possible approach to better understand whether the implicit nature of the deficit is related only to different neural activation or whether this difference is reflected also at a behavioural level. Indeed, preverbal infants lack any kind of top-down compensative strategies. To this end, we investigated infant offspring of adults who show high or low autistic traits.

Autistic traits can be defined as subthreshold impairments in social interaction and communication, like restricted behaviours, interests and activities similar to those seen in individual with a diagnosis of ASD (Constantino, Lajonchere, Lutz, Gray, Abbacchi, et al. 2006). Autistic traits are continuously distributed in the general populations (Constantino et al., 2006; Dawson et al., 2002; Virkud, Todd, Abbacchi, Zhang, and Constantino, 2008) and ASD represents the upper extreme of this continuum of social and communicative difficulties, defined as broad autism phenotype (Constantino et al., 2006). Individuals from the general population with high autistic traits show social and communicative impairment similar to those seen in ASD (Baron-Cohen et al. 2001; Grinter et al. 2009; Happe, 1999; Hudson et al., 2012; Reed et al., 2011; Sutherland and Crewther, 2010) and share genetic susceptibility factors with ASD individuals (Bralten et al. 2017). Additionally, it is reported a heritability rates of autistic traits ranging from 36 to 87% in the general populations (Robinson et al., 2011; Ronald and Hoekstra, 2011). Therefore, studying infants whose

parents show high autistic traits may enhance our understanding of the underlying mechanisms for social and communicative difficulties in ASD.

Given the high heritability of autistic traits (Ronald and Hoekstra, 2011; Robinson et al., 2011), the present study was aimed at investigating whether autistic traits in no-diagnosed adults could be related to abnormalities in visual SL abilities in their 6-months-old infants offspring. To test this hypothesis, we measured the ability to extract visual statistical relationships in two groups of 6-months-old whose parents had respectively low and high autistic traits.

Visual SL is a general domain mechanism functioning in the auditory and visual domains (e.g., Bertels, San Anton, Gebuis, and Destrebecqz, 2016; Kirkham et al., 2002; Saffran et al., 1996; Saffran et al., 1999). Moreover, it presents from birth (Bulf et al., 2011) and has a high degree of continuity across development in typical population (Fiser and Aslin, 2002a, 2002b). Given these characteristics and the critical role played by SL mechanisms in the development of social skills (Monroy et al., 2017; Ruffman et al., 2012), SL could be an ideal early neurocognitive marker for ASD. As said before (in this introduction), only one study had measured visual SL in young children (2 to 6 years of age) with ASD, showing that visual SL is associated with social and communicative skills (Jeste et al., 2015). Conversely, Mayo and Eigsti (2012) showed that linguistic SL ability in ASD school-aged children was not correlated with language ability. As visual SL seems to map better than auditory SL (with linguistic stimuli) the presence of an implicit learning deficit in ASD, we decided to use visual domain to investigate whether the ability to extract statistical relations in a sequence of elements is impaired in preverbal infants at risk for ASD by virtue of having parents who show high autistic traits.

Using the visual habituation task developed by Kirkham et al. (2002), 7-months-old infants were presented with temporal sequences of geometrical shapes. The sequence was composed by 3 pairs of shapes presented in random order, with a transitional probability of 100% between shapes within each pair and a transitional probability of 33% between shapes across pairs. Shapes were presented one at time in the center of the screen in a continuous stream, with no break or delay between shapes. During the test phase, infants were presented with familiar and novel sequences in alternation. Familiar sequence contained the same statistical structure showed during the habituation phase, whereas in the novel sequence shapes were presented in a random order, giving rise to a transitional probability between shapes of 0%. Autistic traits in their parents were measured with a self-report questionnaire, i.e. the Italian standardization (Ruta, Mazzone, Mazzone, Wheelwright, and Baron-Cohen,

2012) of the Autistic-spectrum Quotient (AQ) questionnaire developed by Baron-Cohen et al., (2001). We expected that infants whose parents obtained high scores in the AQ questionnaire (above 1 SD from the mean, HAT group) would have showed a difficulty to extract transitional probability across visual elements respect to their peers whose parents presented low AQ scores (LAT group). In order to match the control group with the experimental one for cognitive development, infants' cognitive skills were assessed using the Bayley cognitive sub-scale (Bayley Scales of Infant Development; Bayley, 2006).

Method

Participants

Two groups of 6-months-old infants have been recruited relying on the scoring obtained by their parents at the AQ questionnaire (Baron-Cohen et al., 2001; Ruta et al., 2012). One group (HAT, N=20) was composed of infants whose parents showed high autistic traits (> -1 SD), the other (LAT, N=20) was composed of infants who had at least one parent with low autistic traits (≤ -1 SD). For the LAT group (8 females) the mean age was 207.68 days (SD = 10.18), and for the HAT group (9 females) the mean age was 217.10 days (SD = 21.36). Nine additional infants have been tested but excluded from the final sample because of general fussiness ($n = 3$), because they did not reach the habituation criterion ($n = 2$), and because their looking times during the test phase were 3 SD above the mean ($n = 4$). All infants that entered in the final sample had biological parents and did not present sensorial or neurological disorder or autism within first-degree relatives. Socio-demographic parental information and perinatal information were collected using ad hoc questionnaires filled out by parents. The inclusion criteria for each infant were gestational age major or equal of 36 weeks, birth weight major or equal to 2500 gr, and a scores in the Bayley cognitive scale major or equal to 7 (Bayley, 2006).

Demographics information of infants and their parents, compared through t-tests (Table 5.1), did not reveal any significant differences between the two groups.

	LAT group (n=20)	HAT group (n=20)	t test		
	Mean (SD)	Mean (SD)	t (df)	p	Choen's d
Gestational age	38.78 (1.52)	39.15 (1.27)	-0.82 (37)	.418	-0.27
Birth weight	3294.72 (467.92)	3279.50 (416.02)	-0.11 (36)	.916	-0.04
Bayley Cognitive sub-scale ^a	11.83 (1.15)	11.80 (1.51)	0.10 (35)	.922	0.03
Mother's age	33.60 (4.58)	34.00 (5.67)	-0.24 (38)	.808	-0.08
Father's age	35.45 (4.47)	34.47 (10.30)	0.39 (37)	.701	0.13
Socioeconomics status ^b	59.25 (11.95)	55.56 (18.46)	0.74 (36)	.464	0.25

Table 5.1. Independent samples t tests were run to compare infant's demographics information between LAT and HAT groups. The t test did not reveal any significant differences between the two groups. (a) Cognitive subscale from the Bayley Scales of Infant Development (Bayley, 2006); (b) Socio-economic status was assessed using the Hollingshead scale. The range score of this scale is between 10, corresponding to unskilled workers, to 90, corresponding to major professional. The score was assigned to each parental job and the higher of two scores was used when both parents were employed (Hollingshead, 1975).

Parents gave written informed consent prior the testing of their infants. The research was approved by Ethical and Scientific Committees of Scientific Institute 'E. Medea' and has been conducted accordingly with the ethical standards of the 1964 Declaration of Helsinki.

General procedure

Assessment of paternal autistic traits

One month prior to the child's 6-month birthday, each parent completed a paper version of the AQ questionnaire (Barhon Cohen et al., 2001; Italian standardization: Ruta, et al., 2012). The questionnaire is composed of 50 items, grouped in 5 sub-scales: social skills, attention switching, attention to details, communication and imagination. The total score is calculated by the sum of the score for each subscale, and it ranges from a minimum of 0 to maximum of 50. Higher scores reveal a presence of autistic traits. Norms are available for Italian adult sample (mean score for fathers = 16.77, SD = 4.61; mean score for mothers = 14.51, SD = 5.17; Ruta et al., 2012). Infants were divided in two groups (HAT and LAT groups) relying on the total standardized score obtained by their parents. An infant became part of the HAT group when his/her parents obtained a score below one SD of the mean (z-score) in the AQ questionnaire. Table 5.2 reported the demographics information, parental scores on the AQ sub- scales, and the total AQ score for the LAT and HAT groups respectively.

		LAT group (n = 20)	HAT group (n = 20)
		Mean (SD)	Mean (SD)
Autistic traits in parents	<i>Social skills</i>	1.57 (1.39)	4.64 (2.43)
	<i>Attention switching</i>	3.32 (1.82)	5.44 (1.50)
	<i>Attention to details</i>	4.64 (2.61)	5.68 (2.32)
	<i>Communication</i>	2.05 (1.58)	4.08 (2.20)
	<i>Imagination</i>	2.52 (1.71)	4.28 (2.05)
	<i>Total AQ</i>	14.11 (3.56)	24.12 (3.96)
	Total AQ Z-score	0.27 (0.68)	-1.80 (0.76)

Table 5.2. Means and standard deviations of the paternal raw scores obtained in the AG questionnaire for the LAT and the HAT groups. Total AQ Z-score was calculated using the Italian standardization of the questionnaire (Ruta et al., 2012).

Infants' statistical learning task

Apparatus and stimuli

The habituation task was run with the software E-prime 2.0 on a 21-inch monitor (resolution 1360x768 pixel) in a sound isolated and dark silent-cabin. The entire experimental session was recorded by a video camera positioned on the top of the monitor to collect infants' looking behaviour. Outside the room, an experimenter viewed the infants on a second monitor and recorded the infant's looking time by pressing a keypress on the computer keyboard. The experimenter was blind to the condition to which each infant was assigned. The program calculated the habituation criteria for each infant and successively presented the test trials automatically.

Stimuli were six colored shapes (turquoise square, blue cross, yellow circle, pink diamond, green triangle, and red octagon) presented one at time in a continuous stream without breaks between shapes. Each shape was showed for 750 milliseconds and loomed from 3 to 10 cm. Following Kirkham et al. (2002), the looming was introduced to maintain infant attention.

Experimental procedure

Infants sat on the parent's laps at a distance of 60 cm from the monitor. The parent was instructed to not interact with the infant to avoid the possibility to a parental influence on the spontaneous infant's interest for the stimuli. An infant-controlled visual habituation task, similar to the one implemented by Kirkham and colleagues (2002), was used. Cartoon animated images accompanied with varying sounds were used as attention getters before the beginning of each trial. As soon as infants looked at monitor, the habituation phase started. Stimuli appeared in a continuous stream in the center of the screen on a black background.

The stimuli were organized into three pairs of shapes presented in a random order, in which the transitional probability between shapes was 100% within each pair and 33% between pairs (Figure 5.1). A trial ended when infants looked away for 2s or looked for more than 60 s. At the end of each trial, an attention getter appeared in the middle of the monitor to re-attract the infants gaze on the stimuli. Infants were habituated to this sequence until they reached the habituation criterion or after a maximum of 12 trials. The habituation criterion was reached when the sum of infants' looking times on three consecutive trials were equal to or less than 50% of the total infant's looking time of first three trials (Slater, Morison, and Rose, 1985). During the test phase, infants viewed 6 test trials in which familiar and novel sequences were presented in alternation, with the order of presentation (i.e., novel or familiar first) counterbalanced among infants. The familiar sequence contained the same relationships between shapes viewed during the habituation phase, whereas in the novel sequence each shape was showed in a random order, with the constrain that only two identical shapes could appear in a row. As a result, transitional probability between shapes in the novel sequences was 0%, ensuring that any difference in looking time between the novel and the familiar sequence would necessarily be related to the statistical structure of the sequences. After each experimental session, the Cognitive subscale of the Bayley Scales of Infant Development was administered for each infant (Bayley, 2006).

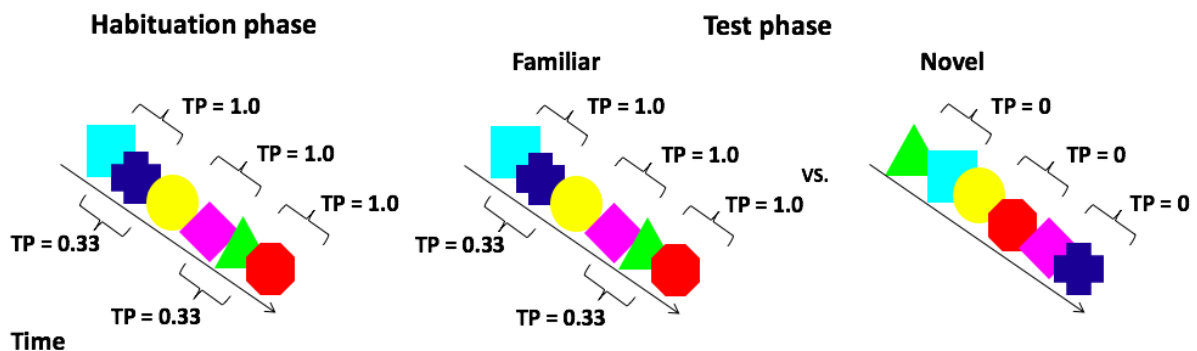


Figure 5.1. Schematic representation of visual SL task

Results

In the visual SL task, all infants within the two LAT and HAT groups reached the habituation criterion. The total number of trials to reach the criteria were similar between groups, with a mean of 6.50 trials (SD = 1.00) for the LAT group and a mean of 7.15 trials (SD = 1.60) for the HAT group; $t(38) = -1.54, p = .133$, Choen's $d = -0.50$. The total looking time of the habituation phase was similar between two groups with a mean of 94.29 s (SD =

52.19) for the LAT group and a mean of 124.41 s (SD = 88.25) for the HAT group, $t(38) = -1.31$, $p = .197$, Cohen's $d = -0.42$. An ANOVA on the habituation looking time with group (LAT vs. HAT) as between-participants factor and mean of looking time of habituation trials (first three vs. last three) as within-participants factor was conducted. The analysis revealed a significant decline in mean looking time from the first three ($M = 70.84$ s, $SD = 8.94$) to the last three habituation trials ($M = 24.64$ s, $SD = 2.80$). $F(1,38) = 45.84$, $p < .001$, $\eta^2 = .547$, confirming that infants successfully reached the habituation criteria in both groups. No other effects or interactions were significant ($ps > .567$).

To compare infants' ability to discriminate the novel from the familiar sequence at test, a repeated measure ANOVA was conducted on infants' looking times toward novel and familiar test trials, with the AQ group (Low AQ vs. High AQ) and first test trial (novel vs. familiar) as between-participants factors, and test trial pair (first vs. second vs. third) and test trial type (novel vs. familiar) as within-participants factors. The analysis showed a main effect of pair $F(2,72) = 5.57$, $p = .006$, $\eta^2 = .134$, whereby looking time was greater in the first pair ($M = 9.06$ s; $SD = 5.72$) than in the second pair ($M = 6.69$ s; $SD = 3.50$), $p = .007$ (Bonferroni correction). Moreover, the ANOVA revealed a Pair x Novelty x AQ group interaction, $F(2,72) = 3.90$, $p = .025$, $\eta^2 = .098$. No other effects or interactions were significant ($ps > .102$). In order to better understand the interaction, two additional ANOVAs were conducted separately for each group (Low AQ vs. High AQ) first test trial (novel vs. familiar) as between-participants factors, and test trial pair (first vs. second vs. third) and test trial type (novel vs. familiar) as within-participants factors. The ANOVA for the Low AQ group revealed a main effect of pair $F(2,36) = 5.99$, $p = .006$, $\eta^2 = .250$, whereby looking times were greater in the first pair ($M = 8.79$ s; $SD = 5.87$) than in the second pair ($M = 6.19$ s; $SD = 3.18$, $p = .030$, Bonferroni correction) and in the third pair ($M = 5.59$ s; $SD = 4.04$, $p = .054$, Bonferroni correction). The ANOVA showed also a main effect of novelty $F(1,18) = 7.45$, $p = .014$, $\eta^2 = .293$, whereby looking times were greater for the novel ($M = 8.06$, $SD = 1.09$) than for the familiar ($M = 5.83$, $SD = .68$) sequences. Finally, a pair X novelty interaction was found, $F(2,36) = 3.84$, $p = .031$, $\eta^2 = .176$. To explore this interaction, t-test comparisons on the looking times to the novel vs. the familiar sequences were run for each of the test pairs, revealing a novelty effect only in the first pair (novel sequence: $M = 11.27$, $SD = 9.16$; familiar sequence: $M = 6.31$, $SD = 4.28$), $t(19) = 2.72$, $p = .014$, Cohen's $d = .69$. No other effects or interactions were significant ($ps > .257$). For the High AQ group, the ANOVA did not reveal any effect ($ps > .123$), demonstrating that in the High AQ group

infants were not able to discriminate between the novel and the familiar sequence at test (Figure 5.2).

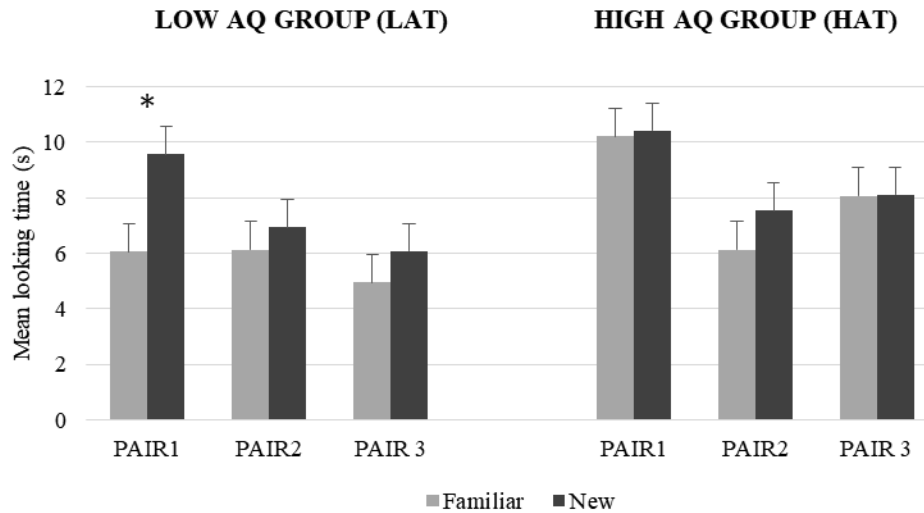


Figure 5.2 Mean looking times (+SE) to the familiar and to novel test trials for the Low AQ group (left side) and the High AQ group (right side). *: $p < .005$.

Discussion

SL is a powerful implicit learning mechanism that allows to track statistical relationships from a continuous string of elements (Saffran et al., 1996). It has been demonstrated that SL is present from birth (Bulf et al., 2011), and that it is a domain general mechanism that operates on natural speech (Pelucchi et al., 2009), non-linguistic auditory stimuli (Saffran et al., 1999), visual sequences (Kirkham et al., 2002) and actions (Monroy et al., 2017; Roseberry et al., 2011). Sensitivity to the input statistical structure has become an important theoretical construct in explaining a wide range of human capacities such as the development of communicative gesture (Alcock, 2006; Bishop, 2002) and, more in general, social learning and social understanding (Lieberman, 2000; Ruffman, 2012). A recent theory postulates that a deficit in SL abilities could be involved in linguistic and communicative problems across a range of developmental disorders such as ASD (Ullman and Pierpont, 2005; Ullman, 2004). Moreover, SL capacities might probably be damaged in individuals with social understanding and communicative subthreshold impairments, such as individuals who show high autistic traits (Hudson et al., 2012).

Given the high heritability of autistic traits (Robinson et al., 2011; Ronald and Hoekstra, 2011), the present study investigated the ability to extract visual statistical

relationship in two groups of 6-months-old whose parents had respectively low and high autistic traits. Using the visual habituation task developed by Kirkham et al. (2002), we assessed infants' ability to discriminate between sequences that contained statistical regularities vs. non-structured sequences. Result showed that only the Low AQ group of infants discriminated between the novel and the familiar test sequences, providing evidence that they have learnt the statistical structure embedded in the habituation sequence. On the contrary, infants that had part of high autistic traits group did not show a preference for structured or random order presentation, suggesting that they were not able to extract the statistical relationships embedded in the visual sequences during the habituation phase. Overall, these results seem to demonstrate that statistical learning ability is impairment in infants whose parents showed subthreshold autistic social difficulties.

This finding is in a line with the recent study of Jeste et al. (2015) in which SL ability was assessed in pre-school age children with a diagnosis of ASD. Jeste and colleagues (2015) measured SL ability using visual stimuli and recording ERPs neural response, ensuring an implicit measure of the functioning of SL mechanism. Indeed, while some studies reported intact SL ability in ASD individuals (e.g., Mayo and Eigsti, 2012), the use of an overt (explicit) behavioural response, along with the use of linguistic material, might have hindered the presence of a SL deficit, as these factors might have activated top-down compensatory strategies. As Jest et al. (2015), the lack of SL abilities in the High AQ infant group was obtained using a visual SL task that was truly implicit, as infants lack any kind of top-down compensatory strategies. Thus, the present finding further accounts for the necessity to use visual stimuli and implicit measures to better understand the functioning of SL mechanism in ASD.

While our data seem to support the idea of a visual SL impairment in ASD, it is worth noting that visual SL in ASD individuals is modulated by the way in which visual information is presented. Indeed, in the presence of a statistical relations based on spatial co-occurrence of pairs of shapes (in which the location of one shape within the pair is determined by the location of the other shape of the same pair) individuals with a diagnosis of ASD showed a superior visual spatial processing than adults of the control groups (Roser, Aslin, McKenzie, Zahra, and Fiser, 2015). Conversely, ASD is related to a deficit in extracting temporal statistical relations between visual elements displayed one at time on the screen (Jeste et al., 2015). This evidence suggests the possibility that SL is not impaired per se in ASD, but it might rather relate to specific constrains in the processing of visual sequences. This, in turn, might have a cascading effect on the impairment of high-level

cognitive functions related to ASD, such as social understanding of others' goals and intentions from a continuous and dynamic sequence of actions. Indeed, the understanding of social actions emerges through the extraction of the temporal and spatial relations embedded in the sequences (Roseberry et al., 2011), and the present findings suggest that temporal SL might be impaired in infants at risk for ASD. A dissociation between ASD individuals' ability to chunk temporal vs. spatial statistical relations is in line with the presence of different processes of analysis for temporal and spatial SL in the general populations (Tummeltshammer et al., 2017).

Overall, our results provide the first behavioural evidence that infants' dysfunctions in visual SL mechanism may be related to subthreshold autistic social impairments in their parents. The lack of SL learning in the High AQ group is particularly relevant considering that in our visual SL task the information about the presence of a structure in the habituation sequences was provided by multiple cues, i.e. frequencies of co-occurrence between shapes and transitional probabilities per se, i.e. the probability that an item X was followed by an item Y (for the role of frequencies and transitional probabilities in modulating infants' SL see Aslin et al. 1999). Even with the presence of this redundant information in specifying the structure of the sequence, the High AQ infants were not able to recognize the familiar sequence during the test phase.

Several limitations of this study should be considered. First, the criterion to be part of the High AQ group was to have at least one parent with a high AQ total score. Since, as already found for ASD (Amaral, Schumann, and Nordahl, 2008; Baron-Cohen, Lombardo, Auyeung, Ashwin, Chakrabarti, and Knickmeyer, 2011), sub-clinical autistic traits are more prevalent in males than in females (Baron-Cohen et al. 2001; Constantino and Todd, 2003), a larger sample of High AQ infants should be tested in order to control whether paternal vs. maternal autistic traits would modulate infants' visual SL ability, and whether parents' gender would interact with the gender of their offspring in affecting infants' performance on the task. Second, as a huge clinical variability has been found within the autism spectrum disorders (Lenroot and Yeung, 2013), a subsequent step of this study will be to create sub-groups of infants based on specific autistic traits, such as difficulties in attention to details, communication, and/or restricted interest (Baron-Cohen, et al. 2001). Third, a longitudinal prospective should be adopted to collect data on the later behavioural outcomes in infants at risk for ASD in order to better understand the developmental trajectory and the individual differences in their social-communicative difficulties. Overall, findings from the present

study account for the possibility to use visual SL as an early neurocognitive marker for broader autism phenotypes and autism spectrum disorders.

CHPATER 6

VISUAL STATISTICAL AND RULE LEARNING IN INFANTS AT HIGH RISK FOR DEVELOPMENTAL DYSEXIA AND SPECIFIC LANGUAGE IMPAIRMENT

As said in the brief introduction of the chapter 5, the investigation of core deficits or ‘intermediate phenotypes’ (like implicit learning mechanisms) in populations at risk for language and communicative disorders might become a successful strategy to identify the complex diagnostic phenotypes earlier in the development. Moreover, it is particularly relevant in SLI, DD, and ASD populations for which the diagnosis is made only after the second year of life.

This last study was aimed to investigate whether visual SL and RL could act as early neuropsychological markers to develop SLI and DD. More specifically, we tested visual SL and RL abilities in 7- and 8-months-old infants with a high family risk to develop DD and SLI. In this chapter I will present the very preliminary data from this study.

Introduction

Specific language impairment (SLI) and developmental dyslexia (DD) are neurodevelopmental disorders in which language and reading, respectively, are delayed (APA, 2013). In most cases, these disorders are not clearly distinct, and both are characterized by a substantial overlap and heterogeneity of reading and linguistic impairments, as reported by recent multiple-component models on the nature of SLI and DD (see Ramus et al., 2013). Indeed, it has been proposed that SLI and DD share language deficits and determinants (Bishop and Snowling, 2004; Catts, Adlof, Hogan, and Weismer, 2005), since they are often in comorbidity and aggregation in the same families, sharing genetic common etiology (Plomin and Kovas, 2005).

Recently, Ullman (2004) proposed the existence of a common implicit learning deficit that could explain the language and learning problems found in individuals with a diagnosis for SLI and DD. This model, called the declarative/procedural model, proposed that the procedural memory system plays a critical role in learning the structure of language. In particular, the procedural memory system would be important to grasp the grammatical structure of language and its sub-components such as syntax, morphology, and an aspect of phonology defined as combination of sounds (see Ullman, 2004). By this model, individuals with SLI and DD could share an impairment in implicit learning abilities that may explain the phonological, morpho-syntactic and syntactic impairments found in these disorders (Cantiani et al., 2013a; Cantiani et al., 2013b; Guasti et al., 2015), despite a spared declarative memory system (Ullman and Pierpont, 2005; Ullman and Pullman, 2015; for more details see Chapter 1, paragraph 1.4). Evidence in literature showed an impairment in implicit learning abilities in children with SLI and in children with DD (for SLI, e.g., Lum, Gelgec, and Conti-Ramsden, 2010; for DD, e.g., Lum et al., 2013). For example, children with SLI were not able to track statistical relationships between speech and non-speech stimuli respect to a control group of typically developing children (Mainela-Arnolds and Evans 2014; Evans et al., 2009). In line with this evidence, adults with DD showed a less efficient SL ability when exposed to linguistic and tone stimuli respect to a control group (Gabay et al., 2015). Overall, these findings suggest that a deficit in implicit learning mechanisms has considerable explanatory power to define the lexical and syntactic deficits that are in overlap between SLI and DD individuals.

The hypothesis that SLI and DD might share a common domain general implicit learning deficit converges with a neuroconstructivist view of atypical development, by which

neurodevelopmental disorders are considered as emerging gradually from innate and domain general neural dysfunctions, that, in turn, constrain the input available to the child (Johnson, 2011; Karmiloff-Smith, 1998;). These initial deficits would have a cascading effect on infants' development, leading to far-reaching atypical outcomes later in development. On this vein, rather than concentrate on the study of disorders solely at their end state in school-aged children and adults, it becomes crucial to place the focus on at risk populations in early infancy, like infants at risk of developing the disorders by virtue of having a familiar predisposition.

To our knowledge, only one study has assessed the implicit learning abilities in 12-months-old infants with a familiar risk to develop DD (Kerkhoff et al., 2013). The authors used a SL-like task, investigating infants' abilities to learn non-adjacent relationships between syllables, which are supposed to resemble grammatical relations between non-adjacent elements in natural language, e.g. between 'is' and '-ing' in 'she is happily singing'. Infants with a family risk for DD and infants without a family risk (low risk to develop DD) were exposed to a string of syllables containing non-adjacent dependencies as a-X-c and b-X-d in which the first and third elements were fixed, while the middle element changed. During the test phase, infants listened familiar and new sequences. The familiar sequence followed the same pattern of non-adjacent relationship presented during the familiarization phase (i.e., a-X-c), whereas the new sequence followed a different pattern (i.e. a-X-d). Results showed that infants at low risk were able to discriminate the novel sequence from the familiar one (novelty preference), while infants at risk for DD did not show any discrimination ability. This finding provides evidence for an impairment in the ability to extract non-adjacent dependencies embedded in a sequence of syllables in infants at risk for DD but not in infants at low risk. Kerkhoff et al. (2013) suggested that the ability to extract statistical relationship from a string of speech elements might be used as an early marker for DD, as an impairment in early SL ability might impact the subsequent development of phonological and syntax skills.

However, this study investigated the ability to track statistical information from auditory stimuli belonging to the linguistic domain. The use of linguistic material in infants with a familiar risk for DD does not allow to understand whether the difficulties in SL abilities are related to difficulties in processing linguistic material or are be related to a SL deficit per se. Indeed, infants at risk to development DD showed difficulties to perform fine-grained acoustic analyses (Cantiani et al., 2016, Benasich and Tallal, 2002) that is critical to the decoding of the speech stream. This evidence accounts to the idea that infants at risk for

DD might have a disadvantage to process statistical relationship from the speech independently from a deficit in statistical learning mechanism. A possible way to disentangle this issue is to test the SL abilities in infants at risk for DD using non-linguistic material, such as sequences of visual elements.

Moreover, Kerkhoff and colleagues (2013) investigated infants' ability to learn non-adjacent repetition, suggesting that this ability is crucial to extract the grammatical structure of language. However, they used speech sequences that did not require any generalization to new items, without considering that one important component of grammatical acquisition is the ability to transfer and generalize the acquired structure to new elements. In literature, there is a debate on whether the ability to track non-adjacent relationships supports both phonological and grammar skills (Aslin and Newport, 2014; Perruchet and Pacton, 2006), or whether it is only responsible for phonological knowledge and a second mechanism drives the extraction and generalization of grammar structure (Endress and Bonatti 2016; Endress et al., 2009). This latter view proposed that statistical learning (SL) allows to learn statistical contingencies between elements and supports the development of phonological skills (Saffran et al., 1996), while rule learning (RL) allows to extract high-order structures and to generalize these rules to new stimuli (Marcus et al., 1999), thus supporting the development of grammar skills (see Chapter 2 for an empirical evidence of the presence of a relation between rule learning abilities in preverbal infants and their later grammatical development).

Capitalizing on this model, we investigate the function of both visual SL and RL in the same group of infants with a familiar risk for SLI/DD as possible early markers for the development of language and reading disorders. To this end, we compared infants with a family risk (with infants without a family risk in a SL (Kirkham et al., 2002) and a RL (Bulf et al., 2017) visual habituation task. Infants with a negative family-history (FH-) defined the control group, while infants with a positive family-history (FH+) defined the experimental group.

The FH+ and FH- group of infants were tested in two different experimental sessions. In the first session, infants were tested at 7 months of age to assess their visual SL abilities. Using the classical visual habituation task developed by Kirkham et al. (2002), infants were exposed to continuous string of six geometrical shapes containing a statistical structure. After the habituation, infants were presented with the statistically structured familiar sequence and with a novel sequence that did not contained statistical cues. In the second session, infants were tested at 8 months of age in a visual RL task. Using the visual habituation task developed by Bulf et al. (2017), infants were habituated with triplets of shapes containing a

non-adjacent ABA rule. During the test phase, infants were presented with ABA (familiar) and ABB (new) rules instantiated by a new set of shapes in order to test their ability to generalize the rule presented during habituation. If infants' SL and RL abilities were intact, they should have discriminated the novel and familiar sequence at test in both the SL and the RL tasks.

Capitalizing on the literature exposed before that found impaired implicit learning mechanisms in SLI (Mainela-Arnolds and Evans 2014; Evans et al., 2009) and DD (Gabay et al., 2015, Sigurdardottir et al., 2017), we expected an impairment of visual SL and RL abilities in the FH+ group, and a spared implicit learning for both SL and RL mechanisms in the FH- group.

The present study is part of a currently on-going longitudinal project aiming at identifying early risk markers for SLI/DD in Italian infants (Cantiani et al., 2016; Piazza et al., 2016; Riva et al., 2017). While the study is still ongoing (see Table 2.1, chapter 2), I will report the very preliminary data collected in these three years in collaboration with the Scientific Institute (IRCSS) 'E. Medea' (Bosisio Parini, Lecco).

Methods

Participants

At this stage of the study, the sample was composed by 29 7-months-old infants that performed a visual SL task divided into 20 infants at low risk (10 females; mean age = 217.50, SD = 18.78) and 9 infants at risk for SLI/DD (4 females; mean age = 207.44, SD = 12.14), and by a second group of 29 8-months-old infants that performed a visual rule learning (RL) task divided into 19 infants at low risk (10 females; mean age = 247.05; SD = 8.76) and 10 infants at risk (4 females; mean age = 242.20; SD = 20.02). Ten additional infants at low risk were tested but excluded from the study due to general fussiness ($n = 6$), or because their looking time during the test phase was 3 SD above the mean ($n = 4$). Notably, due of the fact that some families dropped out, the control groups tested in the first and second tasks are (to date) composed only partially by the same group followed longitudinally ($n = 10$). In the experimental group, we have 9 infants followed longitudinally from 7 to 8 months, and 1 infant tested only in the second task. For the 9 infants tested in both the SL and RL tasks, 1 infant had a positive family history for language impairment, 5 infants for dyslexia and 3 infants for both by virtue of having first degree relative with a certificated diagnosed of SLI and DD. The additional infant tested only in the second task had a positive

family history for language impairment. We are currently going on with the recruitment of infants at familiar risk for SLI/DD, and also with the recruitment of infants without family risk in order to increase the sample size of the infants without family risk followed longitudinally.

Infants were assigned to either a family-history negative (FH-) control group or a family-history positive (FH+) group based on an interview to determine if there was a clinical diagnosis of SLI and DD in first-degree relatives. Infants were assigned to the FH+ group if at least one first-degree relative had a certified (clinical) diagnosis of SLI or/and DD. Infants were assigned to the FH- group if all first-degree relatives did not have a certified diagnosis of SLI and DD. Family were recruited from three hospitals within Lecco and Monza Brianza area (northern Italy). Socio-demographic, prenatal and perinatal information were collected using an ad hoc form filled out by parents. The inclusion criteria for each infant were: (1) gestational age ≥ 37 weeks, (2) birth-weight ≥ 2500 grams, (3) APGAR scores at birth at 1' and 5' ≥ 8 and (4) a Bayley Cognitive Score ≥ 7 , (5) both native Italian-speaking parents, (6) absence of certified diagnosis of intellectual deficiency, sensorial and neurological disorders.

Demographic and clinical characteristics of the two groups are reported in Table 6.1 for the visual SL task presented at 7 months of age and the visual RL task presented at 8 months of age respectively.

Visual SL task at 7 months					
	FH- (N = 20)	FH+ (N = 9)	t (df)	p	Cohen's d
Gestational weeks	38.83 (1.20)	38.75 (0.89)	0.17 (24)	.862	0.07
Birth weight	3294.17 (407.67)	3367.50 (493.70)	-0.40 (24)	.695	-0.16
Bayley Cognitive sub-scale ^a	Not already scored	Not already scored	--	--	--
Mother's age	32.78 (5.72)	31.14 (2.48)	-0.86 (22)	.396	-0.37
Father's age	35.06 (5.79)	35.71 (4.89)	-0.66 (22)	.518	-0.28
Socioeconomics status ^b	59.17 (16.29)	58.57 (15.74)	0.73 (22)	.472	0.31
Visual RL task at 8 months					
	FH- (N = 19)	FH+ (N = 10)	t (df)	P	Cohen's d
Gestational weeks	39.31 (1.29)	39.12 (1.13)	0.36 (25)	.720	0.14
Birth weight	3360.05 (379.78)	3391.25 (480.64)	-0.18 (25)	.858	-0.07
Bayley Cognitive sub-scale ^a	11.42 (1.80)	12.60 (1.51)	-1.76 (27)	.089	-0.68
Mother's age	32.90 (4.36)	35.22 (3.27)	-1.42 (27)	.167	-0.55
Father's age	34.85 (4.15)	36.22 (4.80)	-0.79 (22)	.438	-0.34
Socioeconomics status ^b	66.05 (10.35)	55.00 (19.36)	1.98 (26)	.138	0.78

Table 6.1 Demographic information of infants and their parents. (a) Cognitive subscale of the Bayley Scales of Infant Development (Bayley, 2006); (b) Socio-economic status was scored according to the Hollingshead 9-points scale (Hollingshead, 1975).

The parents gave written informed consent prior the testing of their infants. The research was approved by Ethical and Scientific Committees of the IRCCS 'Eugenio Medea' and it conducted in accordingly with the ethical standards of the 1964 Declaration of Helsinki.

Apparatus and procedure

The first visit at the laboratory was schedule at 7 months. During this first visit, infants performed the visual SL task and the Cognitive subscale of the Bayley Scales of Infant Development (Bayley, 2006). One months later, families were re-contacted and the second visit was schedule at 8 months. During the second visit, infants performed the visual RL task.

The same apparatus was used in the visual SL and RL tasks. Visual sequences were presented with the software E-prime 2.0 on a 21-inch monitor with a resolution of 1360x768 pixel in a sound isolated and dark silent-cabin. The entire experimental session was recorded by two video cameras, one positioned in the silent-cabin and the other collocated on the top of the monitor to collect the infants' looking behaviour. Outside the room, an experimenter viewed the infants on a second monitor and recorded the infant's looking time pressing a keypress on the computer keyboard. The experimenter was blind to condition to which each infant was assigned. The program calculated the habituation criteria for each infant and successively presented the test trials automatically.

Visual SL task procedure

The stimuli and procedure were the same implemented by Kirkham and colleagues (2002), and already described in the previous chapter (chapter 5). Six coloured shapes (turquoise square, blue cross, yellow circle, pink diamond, green triangle, and red octagon) were presented continuously without breaks in the centre of the monitor. The stimuli were organized into three pairs of shapes presented in a random order, in which the transitional probability between shapes was 100% within the pair and 33% between pairs (Figure 6.1). Following Kirkham et al. (2002), infants were habituated to this sequence until the infant reached the habituation criterion or after a maximum of 12 trials. The habituation criterion was reached when the sum of infants' looking times on three consecutive trials were equal to or less than 50% of the total infant's looking time of first three trials (Slater et al., 1985). After the habituation phase, infants viewed 6 test trials in which familiar and novel sequences

were presented in alternation, with the order of presentation (i.e., novel or familiar first) counterbalanced among infants. The familiar sequence contained the same relationship between shapes viewed during the habituation phase, while in the novel sequence each shape was showed in a random order with a transitional probability between shapes equal to 0% (see chapter 5 for more detail of the habituation criteria and procedure).

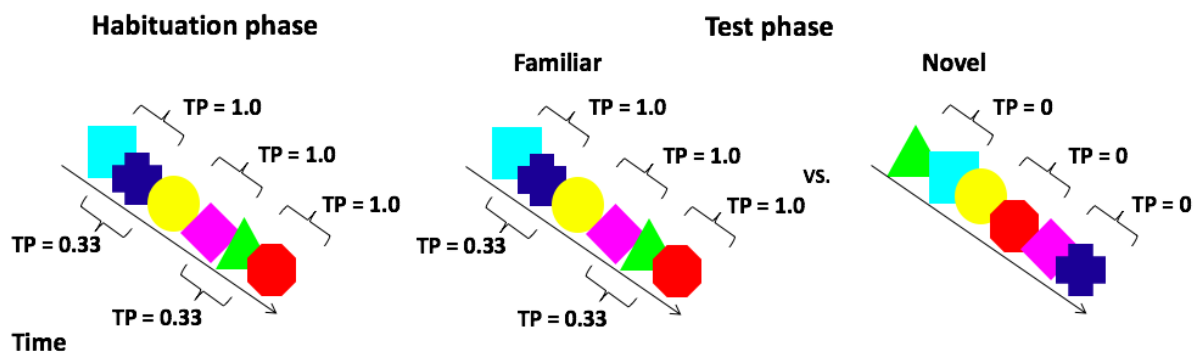


Figure 6.1 Schematic representation of stimuli and procedure of the infants' visual SL task.

Visual RL task procedure

The stimuli and procedure were the same implemented by Bulf and colleagues (2017), and already described in chapter 2. Twelve unique coloured shapes presented on a grey background were used as stimuli (Figure 6.2). The shapes were presented in triplets following an ABA rule (not adjacent repetition of the A element), as in Kerkhoff et al. (2013). Eight unique shapes were presented during habituation, and four different unique shapes were showed during the test phase. For the habituation phase, four shapes were assigned to A group and four to B group, randomly combined by the software (16 ABA sequences). For the test phase four novel shapes were presented, two shapes belong to A group and two to B group, for a total of 4 ABA (familiar patterns) and 4 ABB (novel patterns) (Figure 6.2). Each triplet was shown one at time following a sequential presentation from left to right: the first shape was displayed on the left side of the screen for 330 ms, the second was showed in the middle of the screen for 330 ms, and finally, the last shape was presented on the right side of the monitor for 830 ms. The triads were separated by a 500 ms blank screen, for a 2 seconds total duration of each triplet. Following Bulf et al. (2017), the infants were habituated to this sequence until the infant reached the habituation criterion. The habituation criterion was reached when the sum of infants' looking times on three consecutive trials were equal to or less than 50% of the total infant's looking time of first three trials (Slater et al., 1985) or after

a maximum of 25 trials. After the habituation phase, infants viewed 6 test trials alternating between familiar ABA and novel pattern ABB. The test shapes were different from those presented during the habituation phase. The order of presentation of test trials (i.e., novel vs. familiar first) was counterbalanced across infants.

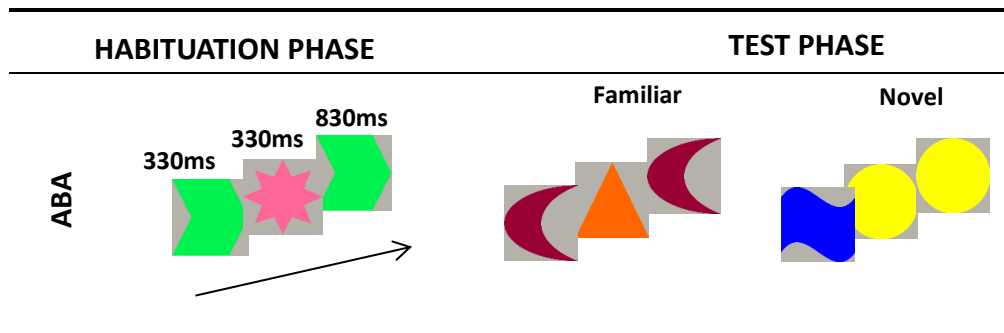


Figure 6.2 Schematic representation of stimuli and procedure of the infants' visual RL task.

Results

At this stage of the project, given the relatively small number of infants with a familiar risk for SLI/DD ($n = 9$), and the fact that the FH⁻ groups were composed only partially by the same infants followed longitudinally, we decided to run two separated ANOVAs on infants' looking times during the test phase for each FH⁺ and FH⁻ group of infants, within the SL task and the RL task. We are still collecting data to increase the samples in order to have much power to directly compare FH⁺ and FH⁻ groups and their performance in the two visual tasks.

Visual SL task

All infants reached the habituation criterion, with a mean of 6.75 trials ($SD = 1.37$) for the FH⁻ group and a mean of 6.89 trials ($SD = 1.36$) for the FH⁺ group, and a total looking time of 86.66 seconds (s) ($SD = 48.91$) for the FH⁻ group and of 93.12 s ($SD = 34.56$) for the FH⁺. To assess that infants of each group reached the habituation criteria, two paired-samples t-tests on the habituation looking time on the first three vs. last three trials were conducted. The analysis revealed for both groups a significant decline in mean looking time from the first three (FH⁻: $M = 21.02$ s, $SD = 15.48$; FH⁺: $M = 18.92$ s, $SD = 11.17$) to the last three habituation trials (FH⁻: $M = 7.30$ s, $SD = 4.31$; FH⁺: $M = 6.81$ s, $SD = 2.73$); $t(19) = 4.96$, $p < .001$, d' Choens = 2.27; $t(8) = 3.37$, $p = .010$, d' Choens = 2.38; confirming that all infants successfully reached the habituation criterion.

To explore infants' statistical learning abilities, two separate ANOVAs for the FH- and FH+ groups were performed on infant's looking time during novel and familiar test trials, with first trial test (novel vs. familiar) as a between-participants factor, and test trial pair (first vs. second vs. third) and test trial type (novel vs. familiar) as within-participants factors. In the FH- group, the analysis showed a main effect of novelty $F(1,18) = 4.29$; $p = .053$, $\eta^2 = .192$, whereby looking time to novel sequences at test ($M = 7.38$ s; $ES = 0.76$) was greater than to the familiar ones ($M = 5.86$ s; $ES = 0.40$). No other effects or interactions were significant ($ps > .2$). In the FH+ group, the analysis revealed a main effect of novelty $F(1,7) = 6.36$, $p = .040$, $\eta^2 = .476$, with greater looking times to the novel sequences ($M = 9.56$ s, $SD = 1.67$) than to the familiar sequences ($M = 5.93$ s, $SD = 1.66$). No other effects or interactions were significant ($ps > .2$).

These results suggest that either in the control and in the experimental group infants were able to extract the statistical structure embedded in the visual sequences (Figure 6.3).

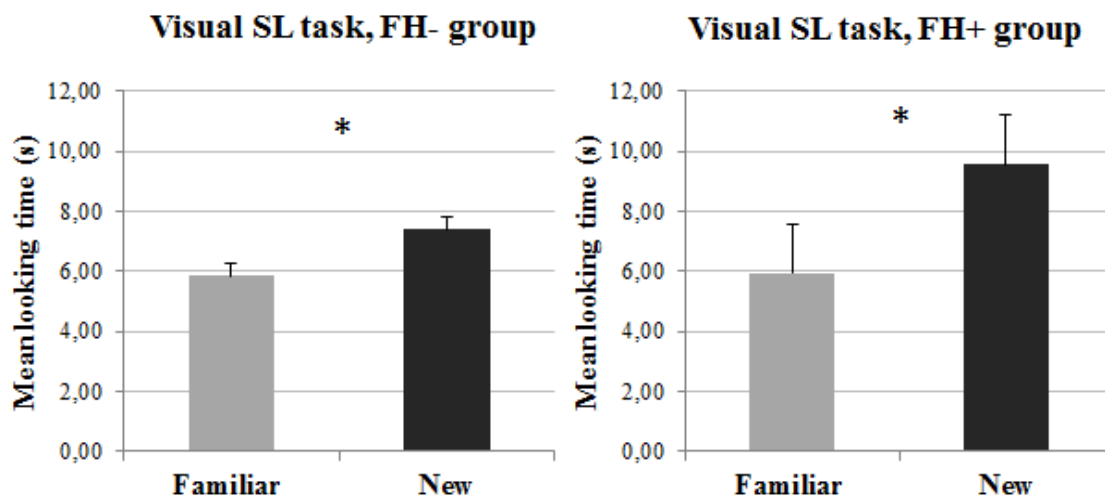


Figure 6.3 Mean looking time to the novel and familiar test sequences in the visual SL task for the FH- group (left side) and FH+ group (right side). *: $p < .005$.

Visual RL task

All infants of FH- group reached the habituation criterion with a mean of 10.05 ($SD = 4.06$) trials, and a total looking time of 66.75 s ($SD = 30.83$). In the FH+ group, all infants reached the habituation criterion, with a mean of 7.60 s ($SD = 2.27$) trials and a total looking time of 67.19 s ($SD = 32.12$). Paired-samples t-tests confirmed a significant decline in mean looking time for each group from the first tree (FH-: $M = 9.02$ s, $SD = 4.36$; FH+: $M = 13.36$ s; $SD = 4.34$) to the last three habituation trials (FH-: $M = 3.67$ s, $SD = 1.51$; FH+: $M = 5.64$

s; SD = 3.08), $t(18) = 7.76, p < .001, d'_{\text{Choens}} = 3.66$; $t(9) = 5.63, p < .001, d'_{\text{Choens}} = 3.75$, demonstrating that the habituation criterion was reached in both FH+ and FH- groups.

For each group of infants, we run an ANOVA on looking times at test with first trial test (novel vs. familiar) as a between-participants factor, and test trial pair (first vs. second vs. third) and test trial type (novel vs. familiar) as within-participants factors. In the FH- group, the ANOVA revealed a main effect of novelty, $F(1,17) = 70.94, p = .012, \eta^2 = .320$, as infants looked more at the new test sequences ($M = 5.81 \text{ s}, ES = 0.84$) than at the familiar ones ($M = 4.17 \text{ s}, SD = 0.46$). No other effects or interaction were found ($ps > .1$), providing evidence that infants with typical development were able to extract and generalize the high-order rule presented during the habituation phase. In the FH+ group, the ANOVA did not reveal any significant effect $ps > .1$, as infants looked equally at the novel ($M = 6.71, ES = 1.34$) and the familiar ($M = 5.83, ES = 1.64$) test sequences, $F(1,8) = 0.65, p = .442, \eta^2 = .076$. Therefore, results from the FH+ suggests that infants at risk for SLI/DD were not able to discriminate between the new and the familiar rules during test (Figure 6.4).

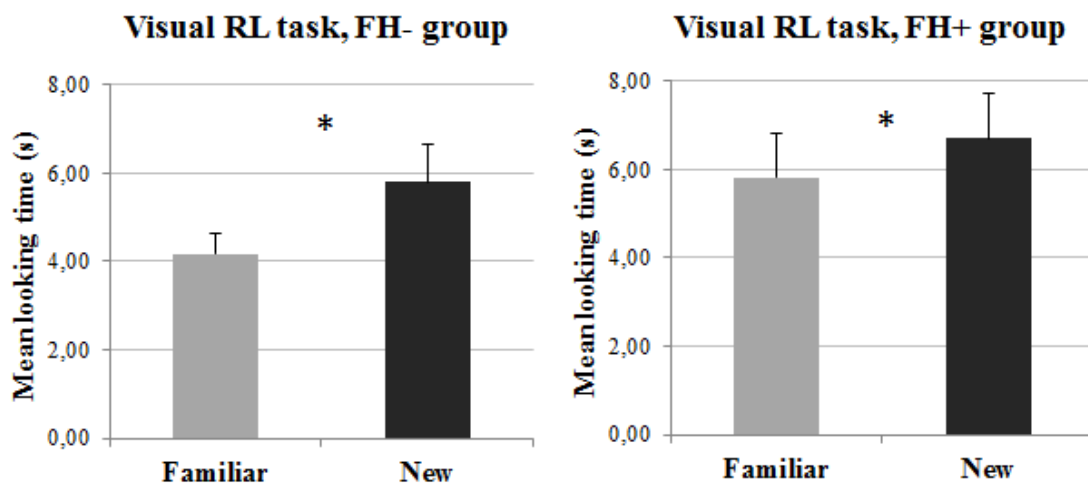


Figure 6.4 Mean looking time during test phase of RL task to new and familiar stimuli for FH- group (left side) and FH+ group (right side). *: $p < .005$.

Discussion

In the present study, we investigated whether the domain-general abilities to track statistical relationship (SL) and to extract and generalize high-order structures from visual sequences (RL) may act as early neurocognitive markers to characterize the typical and atypical development trajectories of language and reading disabilities.

To this end, we tested infants with a family risk for SLI and DD (FH+) and typically development infants (FH-) in a visual SL and a visual RL habituation tasks. In the visual SL

task, 7-months-old infants were exposed to a sequence of shapes in which the probability that an element was predicted by the previous one in the sequence could be 1.00 or 0.33. During the test phase, infants' ability to learn the statistical structure of the habituation sequence was defined with the ability to discriminate between a familiar (that had the same structure of the sequence presented in the habituation phase) or a novel sequence (that lacked any statistical structure). In the visual RL task, 8-months-old infants were exposed to triplets of shapes organized into a non-adjacent pattern (ABA). After the habituations phase, new (ABB) and familiar (ABA) rules were presented using a novel set of elements to test the ability to generalize the habituation pattern. Results showed that in the visual SL task both the FH- and the FH+ groups looked more at the novel than at the familiar test sequences, revealing an intact SL ability. In the visual RL task, only the FH- infants showed a discrimination ability (with a novelty preference) during the test phase, providing evidence that they were able to extract and generalize the rule learnt during the habituation phase. Conversely, the FH+ group did not discriminate between the novel and familiar test sequences, suggesting an impairment in their ability to learn high-order rules from a sequence of visual elements.

On one hand, our data replicate the findings of Kirkham et al. (2002) and Bulf et al. (2017), showing that 7- to 8-months-old infants are able to extract statistically-based and rule-based structures from a sequence of visual elements. On the other hand, the present results suggest that infants at risk for SLI/DD showed a difficulty in learning and generalize high-order rules despite a spread visual statistical learning ability. While our data are very preliminary, they seem to suggest that visual SL and RL mechanisms might play a distinct role in the development of language disorders, as SL seems to be preserved in infants at risk, while RL seems to be impaired.

The present evidence of a preserved visual SL mechanism in infants at risk for SLI/DD is in contrast with those studies that have investigate the functioning of statistical relations embedded in a speech sequence in individuals diagnosed for SLI and DD. Indeed, Evans and colleagues (2009) showed that SLI children were worse in extracting transitional probabilities from a sequence of linguistic stimuli than their typically developing peers after 21 minutes of familiarizations phase, enhancing their performance only when they were familiarized for 42 minutes. Similarly, it is reported that adults with DD were less able to track transitional probability from linguistic stimuli than a control group, even though their performance was above chance (Gabay et al., 2015, Sigurdardottir et al., 2017). Therefore, it seems that the SL ability is less efficient in both SLI and DD, and this evidence seems to be confirmed by the lack of any SL abilities in infants at risk for DD (Kerkhoff et al., 2013). The

difference between these studies and our results might be explained by the use of linguistic vs. visual stimuli. Most probably, linguistic material hinders SL abilities in DD and SLI individuals. On this account, SL might be spared in SLI and DD, but its functioning is altered when diagnosed individuals are requested to process speech sequences. This idea seems to be confirmed by a recent study that found that children with DD are not impaired in their visual sequential learning abilities (Nigro et al., 2015). This latter study revealed also that, even though children with DD can learn regularities from a visual sequence, they are not able to transfer the information that they have learnt to novel instances. This is exactly what we have found in our visual RL, where infants at risk for SLI/DD were not able to generalize the acquired information to novel stimuli.

Overall, our study accounts for the presence of a dissociation between visual SL and visual RL abilities in DD: while visual SL seems to be preserved, visual RL seems to be impaired. As it has been proposed that SL and RL mechanisms are linked to different components of linguistic development, i.e. phonological development vs. grammatical development, the impairment in visual RL abilities in infants at risk for SLI and DD confirms the hypothesis that a mechanism linked to the extraction of grammar structures could be an early marker to development both language and reading problems (Kerkhoff et al., 2013; Ramus et al., 2013; Ullman and Pierpont, 2005;), and further account for the presence of a link between RL abilities and grammatical development (see also chapter 2 for a relation between early visual RL abilities and later grammatical development in typical development infants). It is worth noting, however, that the different results that we have obtained on the SL and RL tasks in the FH+ group might have been due to low-level factors. Indeed, SL sequences contained multiple cues for the extraction of the embedded structure (i.e. frequency of co-occurrence and transitional probabilities) that might have facilitated infants' learning with respect to the visual RL task. Further research should explore this account isolating transitional probabilities from the frequencies of co-occurrence.

The present study highlights the potential role of visual implicit learning mechanisms as early markers for an atypical language development. The investigation of the implicit learning mechanisms at early stages of development and the use of visual material allow to better understand the mechanism underlying complex abilities as language, independently by the culture, education and other environmental confounders. The current findings, if confirmed, might have strong implications for the implementation of early intervention programs based on visual learning training in infants at risk for DD and SLI.

CONCLUSION

One of the central issues in the study of neurodevelopmental disorders is the investigation of domain-general cognitive abilities that could underlie complex clinical phenotypes. To this end, the declarative/procedural model proposes that impairments in implicit learning mechanism might underlie language and communication disorders, as this mechanism allows to extract the rule-based structure of a sequence of elements, an ability that is at the basis of language processing in general, and of syntax and phonology processing in particular (Ullman and Pierpont, 2005). On this vein, a common impairment in implicit learning ability could underlie language and behavioural deficits that characterized specific language impairment (SLI), developmental dyslexia (DD) and autism spectrum disorders (ASD) (Ullman, 2004, 2016; Ullman and Pullman, 2015; Lum et al., 2010). Several studies have investigated the role of implicit learning abilities in determining the deficits that characterized these populations, suggesting that the functioning of implicit learning has considerable explanatory power to define both typical and atypical development (chapter 1, paragraph 1.4).

Implicit learning is a complex and heterogeneous construct, composed by many different types of learning mechanisms, and the present thesis has focused on the role of statistical and rule learning mechanisms. Statistical learning (SL) refers to the ability to extract statistical regularities from a continuous stream of elements (Saffran et al., 1996), while rule learning (RL) allows to detect and generalize abstract rule-like patterns and to generalize them to novel items (Marcus et al., 1999). These mechanisms seem to map different components of linguistic development, i.e. phonological and syntactic skills respectively (Endress et al., 2009; Perruchet and Pacton, 2006; Saffran et al., 1996), and it has been recently proposed that they are crucial for the development of social understanding (Lieberman, 2000; Ruffman et al., 2012).

Here, I suggest the importance of investigating whether and how different types of learning mechanisms are related to different typical and atypical outcomes in language and communication development. On this account, the aim of the present thesis was to investigate whether visual SL and RL abilities can account for different linguistic and communicative outcomes in typical and atypical development, i.e. in SLI, DD and ASD. To this end, we use four different approaches: 1) the study of typically developing infants; 2) the study of diagnosed children; 3) the study of infants at low risk to develop language and

communicative disorders by virtue of having parents with sub-threshold high traits; 4) the study of infants with a family risk to develop language and communicative disorders defined as having a first degree with certified diagnosis.

Our results confirmed the idea that a deficit in general implicit learning mechanism might be involved in SLI, DD and ASD. For example, the study on children with DD (chapter 4), revealed a difference in visual RL ability between children with DD and typically developing (TD) children and we found that this ability is related with grammar comprehension and even reading skills. This result is confirmed by infants at family risk for ASD and SLI/DD (chapter 5 and 6 respectively): visual SL has been found to be impaired in infants at family risk to develop high autistic traits, while visual RL appears to be compromised in infants at risk to develop SLI and DD, despite an intact visual SL ability.

More specifically, the findings of the present thesis suggest three major conclusions. Regards visual RL ability, results across studies appear to converge in the same direction, as they suggest that the ability to extract and generalize high order rules is involved in grammar acquisition. Indeed, the first study (chapter 3) showed that visual RL ability assessed in 7-months-old infants predicts grammatical production at 2 years of life. In line with this data, the study carried out in children with DD (chapter 4) provides evidence for a link between visual RL ability and grammatical skills in childhood. Indeed, children with DD, who has been shown to manifest a deficit in morpho-syntactic and syntactic skills (Cantiani et al., 2013a; Cantiani et al., 2013b; Guasti et al., 2015), demonstrated less efficient RL ability than their peer with a typical development. This latter finding further indicates that a visual RL impairment could be correlated to language damages that characterized individuals with DD. Moreover, correlations analyses conducted on the entire sample of children, revealed a relationship between visual RL and syntax skill. Finally, the idea that visual RL might mediate the development of grammar skill is indirectly confirmed by the study with infants at risk for SLI/DD (chapter 6), who showed to lack any visual RL ability.

Another important aspect revealed by our findings concerns the different functioning of visual SL ability in infants at risk for ASD and SLI/DD. Infants at (low) risk to develop ASD – as their parents showed high autistic traits - were unable to extract statistical relationships across visual elements (chapter 5). Conversely, infants at family risk for SLI/DD seem to be able to learn visual SL relations, as their performance did not differ from a control group of typical development infants. These findings account for the possibility that visual SL might serve as a possible early precursor or mediator of the social and communicative impairments that defined ASD, but seem to be unable to map the early risk in language and learning

disorders. However, it is worth noting that a recent study demonstrated that infants at risk for DD are not able to learn the statistical relations embedded in sequences in the presence of linguistic materials (Kerkhoff et al., 2013). Thus, the difference found in infants at risk for ASD vs. infants at risk for SLI/DD could be due to the fact that we have assessed the SL ability using visual stimuli. Indeed, visual SL has been shown to map better than linguistic SL the presence of an implicit learning deficit in ASD (Jeste et al., 2015, Mayo and Eigsti, 2012), while SL abilities in infants at risk for SLI/DD are altered solely when speech sequences are used (Evans et al., 2009; Kerkhoff et al., 2013, Mainela-Arnolds and Evans, 2014). Future researches should compare directly infants at risk for ASD and SLI/DD using both speech sequences and visual sequences.

Finally, it is worthy to consider the difference in performance between the visual SL and RL tasks within the group of infants at risk for SLI/DD. While visual SL seems to be intact in this population, visual RL seems to be impaired. However, this difference might be due to low-level factors instead of being due to a difference in SL and RL mechanisms per se. In fact, differently from RL visual sequences, SL visual sequences contained multiple cues for the extraction of the embedded structure - i.e. frequency of co-occurrence and transitional probabilities - that might have facilitated the infants' learning with respect to the visual RL task. Further research should explore this account isolating transitional probabilities from frequencies of co-occurrence.

Overall, the present findings suggest that an impairment in visual implicit learning abilities might underlie the development of SLI, DD and ASD, and suggests that visual SL and RL mechanisms might be involved in different types of developmental disorders. In fact, it seems that visual SL is more related to impairments in communicative skills (ASD), while visual RL is more related to impairments in linguistic skills (DD and SLI). Moreover, it is worth to note that one of the main innovative aspects of the present project is the investigation of two implicit learning mechanisms in the same sample of infants at risk for SLI/DD (chapter 6), suggesting that specific sub-components of implicit learning mechanisms, i.e. visual SL vs. visual RL, are differently involved in the development of these disorders. These evidences suggest that, instead of considering the implicit learning as a whole construct, future researches should focus on the way in which different learning mechanisms operate in different linguistic and communicative developmental disorders, as well as explore the way in which tiny variations in the functioning of the same mechanisms are related to different disorders.

In line with the procedural/declarative and the neuroconstructivist models, further investigations should adopt a multifactorial and longitudinal approach in order to better characterize the heterogeneity of deficits within SLI, DD, and ASD, and to investigate at what point the path of development diverges (D'Souza, D'Souza, and Karmiloff-Smith, 2017).

Future directions

An important issue that should be further explored within the relation between implicit learning and developmental disorders is whether the characteristics of stimuli, e.g. visual vs. linguistic stimuli or social vs. non-social stimuli, can differently modulate the functioning of SL and RL mechanisms depending on types of diagnosis. For example, we have recently tested whether visual RL abilities in high functioning autistics are affected by the social nature of the stimuli embedded in the sequences. To this end, we used the same paradigm implemented to investigate visual RL ability in children with DD (chapter 4), but in this case we presented sequences of geometrical shapes, upright-faces, and inverted faces. Preliminary results from this study (that is still ongoing) suggest that high functioning children are able to learn high-order rules from non-social sequences of shapes and inverted faces, but they failed in the presence of visual sequences of upright faces.

Moreover, we have already planned to follow longitudinally the infants at risk for ASD and SLI/DD in order to understand how many of them will develop the disorder. For this reason, infants at risk for ASD will be re-tested with the 'Autism Observation Scale for Infants' (AOSI) scale (Bryson, Zwaigenbaum, McDermott, Rombough, and Brian, 2008) in order to assess their communicative outcome at 18 months of age. In the same way, we will measure the linguistic outcome at 24 months of age in infants at risk for SLI/DD using 'Primo Vocabolario del Bambino (PVB), Parole e Frasi' (Caselli and Casadio, 1995; Fenson et al., 1993). The measure of the developmental trajectory of these infants at risk will be extremely informative to understand whether and how individual differences in performing the visual SL and RL tasks at early stage of development are linked to the emergence of a specific disorder later on development. As this project is part of broader longitudinal project carried out at the IRCCS 'E. Medea' (Bosisio Parini, Lecco) with the aim to investigate early markers for SLI and DD in a multi-factorial prospective, these follow-up measures will also allow to understand the putative role of different early markers, i.e. rapid auditory processing

(Cantiani et al., 2016) and implicit learning abilities, in the emergence of communicative and linguistic disorders.

Finally, in collaboration with the UCLA baby lab of the University of California Los Angeles, we are currently investigating infants' ability to extract multi-layered sequences. This latter study is crucial to understand the specific role of SL and RL information in driving infants learning of complex sequences and, especially, in language acquisition. Indeed, in the real words infants and adults are required to compute fine analysis on complex multi-layered structures characterized by both adjacent and non-adjacent relationships. For example, in natural language the relative clauses as 'The dog that chases the cat is barking,' required to track non-adjacent dependency across phrase that are linked between them. The ability to track adjacent and not adjacent relationships at the same time is relevant to understand the meaning of the sentences and it is reported to be impaired in children with diagnosis of SLI, DD and ASD (e.g., Arosio, Panzeri, Molteni, Magazù, and Guasti, 2017; Durrleman, Burnel, and Reboul, 2017). While this ability was investigated in adults from general populations (for more details see Romberg and Saffran, 2013), to our knowledge there are not studies that have investigated this type of sequential learning in infancy. Using an eye-tracker system within a visual habituation paradigm, we are investigating 9- to 15-months-old infants' ability to learn multi-layered grammar from a-X-b visual sequences that contain statistical dependencies between adjacent and not adjacent elements. Specifically, we are investigating whether infants are able to extract adjacent or non-adjacent dependencies at the same time or whether they focus on one layer at time, parsing adjacent rather than non-adjacent dependencies or vice versa. Preliminary results showed that 9-15-months-old infants are able to extract non-adjacent than adjacent dependencies when they are exposed to multi-layered structures. The next step will be to assess the ability to extract multi-layered sequences in infants at risk for SLI and DD.

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ACKNOWLEDGEMENTS

I would like to sincerely thank my supervisor Prof. Hermann Bulf for his emphatic and professional support, positivity and guidance. I consider myself very fortunate to have had the opportunity to learn from and work with such a fantastic researcher and person. In particular, Dr. Chiara Cantiani and Dr. Valentina Riva were incredibly influential during the infancy of my research and to my growth as a researcher. Thanks too to the undergraduates students, Elena Maria Riboldi and Sara Buonamassa, who assisted me in collection data facilitating my work.

I would also like to thank Prof. Scott Johnson for the great experience of research that I had spent at the UCLA baby lab (University of California Los Angeles).

My deep gratitude goes also to all participants and their families that donate time to participate in the studies. Finally, I must thank my family who have encouraged and endured me throughout my studies.