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Neural correlates of vocal learning in songbirds and humans

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Citation

Kant, A. M. van der. (2015, January 28). *Neural correlates of vocal learning in songbirds and humans*. Retrieved from <https://hdl.handle.net/1887/31633>

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Author: Kant, Anne Marie van der

Title: Neural correlates of vocal learning in songbirds and humans : cross-species fMRI studies into individual differences

Issue Date: 2015-01-28

CHAPTER 6

Reflections of individual differences in grammar learning on the language network

How do individual differences in structural and functional connectivity in the human language network influence adult language learning? Both structural and functional connectivity have been reported to show deficiencies in patients with cognitive or language disabilities. However, few studies to date have studied how individual differences in brain connectivity relate to language learning abilities in healthy participants. The present study employed a combination on functional connectivity analysis of resting-state fMRI (rs-fMRI) and Diffusion Tensor Imaging (DTI) in order to investigate the relation between individual differences in brain connectivity and artificial grammar learning ability. Results showed that both structural and functional connectivity between left hemisphere IFG Pars Triangularis, part of Broca's area, with posterior regions in the language network correlated with the ability of individual participants to acquire an artificial grammar. These results suggest that individual differences in brain connectivity, especially between Broca's area and other regions important for language processing, underlie individual differences in language learning abilities.

6.1 Introduction

Although we share our ability for vocal learning with other species, humans are unique in their ability to spontaneously learn language, which exhibits a complex syntactic system. Learning the syntactic system of our native language takes up a large part of our development and is a fragile process, which

can be impacted by developmental disorders or brain trauma. Human infants are equipped to acquire a highly complex syntactic system without instruction, whereas adult learners have more difficulties acquiring a new grammatical system and show considerable individual differences in the ability to acquire new syntactic structures.

How do individual differences in the human ability to learn a new grammar relate to the neural systems subserving language processing? In a previous fMRI study (see Chapter 5), including the same group of participants that was included in the present study, participants listened to phrases from an artificial grammar containing non-adjacent dependencies, followed by a grammatical judgement task. FMRI results showed a correlation between activation in the Left Inferior Frontal Gyrus (LIFG), the bilateral Superior Temporal Gyri and the bilateral Insulae and the ability to reject violations of the grammar in the grammatical judgement task. A similar effect was found in one of our previous studies assessing the perception of learned vocalizations in zebra finches, a songbird species (see Chapter 3. Individual differences in song learning were found to be reflected in activation of the auditory midbrain in response to auditory exposure to the learned vocalizations.

In humans, A growing body of literature shows that LIFG is an important brain region for syntactic processing in both natural language processing and artificial grammar learning (e.g. Folia & Petersson, 2014; Petersson et al., 2012; Petersson & Hagoort, 2012; Uddén & Bahlmann, 2012; Yang & Li, 2012). Our previous results suggest that activity in a large part of the network involved in language processing underlies individual differences in artificial grammar learning and possibly natural language learning abilities.

However, the brain operates in large-scale interconnected networks rather than individual regions. Moreover, the possibility that individual differences in the ability to learn this specific artificial grammar, containing dependencies between non-adjacent elements, were purely task-related, cannot be excluded based on the fMRI data. The neural basis of individual differences of artificial grammar learning should thus be investigated on the network level, rather than in isolated brain regions. In order to assess whether artificial grammar learning is related to individual differences in connectivity within the language network (Lohmann et al., 2010), we employed resting-state functional MRI (rs-fMRI) and Diffusion Tensor Imaging (DTI) to assess functional and structural connectivity between LIFG, including Broca's area and temporal and parietal language processing regions, including Wernicke's area. Functional connectivity changes induced by auditory exposure to the artificial grammar will be assessed by acquiring rs-fMRI data both before and after participants listen to the artificial language. Resting-state functional connectivity has been shown to reflect structural connectivity (Greicius, Supekar, Menon, & Dougherty, 2009). However, structural connectivity alone does not differentiate between inhibitory and excitatory connections, while functional connectivity between two regions does not necessarily mean there is a direct white

matter connection between the two. By combining DTI and rs-fMRI measurements, we aim to arrive at a detailed analysis of how connectivity within the language network is related to artificial grammar learning.

Prior studies have uncovered links between functional and structural connectivity and language impairments as well as individual differences in language functions of healthy participants. Individual differences in reading (Koyama et al., 2011) as well as learning words from an unfamiliar language (Veroude et al., 2010) have been associated with resting-state functional connectivity differences, while white-matter integrity was shown to be related to artificial grammar learning success (Flöel, De Vries, Scholz, Breitenstein, & Johansen-Berg, 2009). In patients diagnosed with primary progressive aphasia, impairment of syntactic comprehension was shown to correlate with the amount of damage to the left hemisphere dorsal language pathway (Wilson et al., 2011), while autistic individuals with language impairments exhibit decreased functional connectivity (e.g. Kana, Keller, Cherkassky, Minshew, & Just, 2006). We aim to show how functional and structural connectivity together might subservise artificial grammar learning in healthy adults.

The interconnected network subserving language processing and speech production in the left hemisphere shows different pathways (Saur et al., 2008), which subservise different language processing functions. A ventral pathway connects LIFG with anterior temporal regions through the Extreme Capsule, while a dorsal pathway connects LIFG to parietal and posterior temporal regions through the Superior Longitudinal and Arcuate Fasciculi. Prior rs-fMRI data have shown that functional connectivity of language-related regions along these pathways is highly reproducible across participants (Tomasi & Volkow, 2012). Furthermore, several studies (for a review, see Friederici & Gierhan, 2013) have shown that the dorsal language pathway subserves complex syntactic operations. Therefore, individual differences in artificial grammar learning are mainly expected to be related to differences in structural connectivity in the Arcuate or Superior Longitudinal Fasciculus. Functional connectivity between regions connected by the dorsal pathway is also expected to reflect individual differences in artificial grammar learning. Additionally, functional connectivity within the language network is expected to show a larger increase between sessions acquired before and after exposure to an artificial grammar in participants who were more successful at learning the grammar.

6.2 Methods

6.2.1 Ethical statement

All participants gave written informed consent prior to inclusion in this study and were financially compensated for their participation. In accordance with Leiden University Medical Center (LUMC) policy, all anatomical scans were

reviewed by a radiologist. No anomalous findings were reported. All experimental procedures were conducted under approval of the Medical Ethical Committee of the Leiden University Medical Centre, The Netherlands (CME no. NL42690.058.12).

6.2.2 Participants

For the present study, the same participants were included that participated in the study described in Chapter 5. This group consisted of twenty healthy adult volunteers (12 males, 8 females, mean age 28, range 18-43). All participants were right-handed and reported no history of speech- or language disorders, other cognitive impairments or neurological damage. All participants were native speakers of Dutch.

6.2.3 Imaging Procedure

All imaging data were acquired at the LUMC using a 3 Tesla Philips Achieva TX MRI system (Philips Healthcare, Best, The Netherlands) with a whole-head receiver coil. Participants completed a safety questionnaire to screen for counter-indications before scanning. In order to minimize movement, cushioning was placed around the head and for the DTI scan participants were informed about possible vibrations in the scanner bed prior to scanning. Ear plugs and headphones were provided for hearing protection.

Resting-state (rs) fMRI time-series were acquired prior to and after auditory exposure to an artificial language containing non-adjacent dependencies and a control language in order to determine how artificial grammar learning influences functional connectivity between brain areas known to be involved natural language processing. Furthermore, Diffusion Tensor Imaging (DTI) data were acquired to assess differences in structural connectivity between participants that could be related to grammar learning ability. The extent to which participants were able to acquire the rules of the grammar they were exposed to was measured using a grammatical judgement task which took place in the scanner after the second rs-fMRI session. A detailed description of the stimuli and the procedures of both the exposure phase and the grammatical judgement task can be found in Chapter 5.

For each participant, two rs-fMRI sessions (single-shot GE-EPI, 160 repetitions containing 38 transverse slices, TR/TE: 2200/30 ms, voxel size: 2.75 mm³ including a 10% inter-slice gap, FOV: 220 x 217.25 x 104.5 mm) were acquired (before and after exposure). During the 8 min resting state scans, participants were instructed to lay with their eyes closed and to relax, but to not fall asleep. Furthermore, a gradient-echo diffusion weighted scan (60 slices, slice thickness: 2.1 mm, FOV: 224 x 126 x 224 mm) was obtained with diffusion gradients applied in 33 directions with a maximum b value of 1000 s/mm² and one image with $b = 0$ s/mm² (60 slices, TR/TE: 6250/70 ms, voxel size: 2.07 x 2.12 x 2.1 mm with no inter-slice gap, FOV: 224 x 224 x 126 mm).

In addition to the rs-fMRI and DTI scans, a high-resolution 3D T_1 weighted anatomical scan (140 slices, TR/TE: 9717/459 ms, flip angle: 80° , voxel size: $0.875 \times 0.875 \times 1.2$ mm, FOV: $224 \times 168 \times 177.3$ mm) was acquired for each participant to allow for a good-quality registration between participants and normalization of all participant data to the Montreal Neurological Institute (MNI) template.

6.2.4 Resting State fMRI Data analysis

Pre- and post-exposure resting state fMRI data were preprocessed and further analyzed for ROI-to-ROI functional connectivity using the MatLab based CONN functional connectivity toolbox (Whitfield-Gabrieli & Nieto-Castanon, 2012).

The first ten images of each rs-fMRI session were discarded to allow for T_1 equilibration. The remaining images were then band-pass filtered over a low frequency window of interest (0,008-0,09 Hz), removing physiological noise and scanner magnetic field drift. They were then detrended, despiked and convolved with a gaussian kernel. Confounding signal from white matter and CSF (five dimensions) as well as movement (six dimensions) and session effects (one dimension per session) were regressed out. Global signal was not removed, because a large portion of the global signal originates from neuronal activity (Schölvinck, Maier, Frank, Duyn, & Leopold, 2010).

Separate conditions were defined for the pre- and post-exposure sessions. Except the one representing Wernicke's area, all seed ROI's selected for first-level analysis were based on the Brodmann atlas included in the CONN toolbox. Based on the large body of research concerning the network involved in language processing, we included left hemisphere (LH) Brodmann's areas (BA) 44 and 45 (Broca's area), LH BA 39 and 40 (angular gyrus and supra-marginal gyrus) and LH BA 22 (superior temporal gyrus). To seed Wernicke's area, which spans a number of BA's (Tomasi & Volkow, 2012), we placed a 10 mm spherical ROI at MNI coordinates -51 -51 30 (based on Tomasi & Volkow, 2012). Our analyses were focused on left Pars Triangularis of the Inferior Frontal Gyrus (BA 45), because this area has proven to be important for syntactic processing or (for a review, see Friederici & Gierhan, 2013). Bivariate ROI-to-voxel correlations for the pre- and post-exposure conditions were then computed based on the General Linear Model.

Correlation maps for each participant, session and ROI were then entered into a second-level random-effects analysis to test for functional connectivity on the group level. Second-level covariates were defined for age, sex and behavioral measures obtained during the grammatical judgement task and behavioral post-tests. Because the number of rejected violations during the grammatical judgement task was shown to correlate with individual differences in neural activation during listening (see Chapter 5) regression analyses focused on this measure. Pre- and post-exposure networks for the seeds in Broca's and Wernicke's area were computed and further regression analyses

were masked with the sum of these networks. All functional connectivity results discussed in the results section are computed two-sided and reported as FWE-corrected for multiple comparisons (based on Gaussian Random Field Theory, Worsley et al., 1996) on the cluster level with FWE-corrected clusters $p < 0.05$ considered statistically significant. Only voxels with an uncorrected p -value < 0.001 were included in the cluster statistics.

6.2.5 DTI Data analysis

Diffusion-weighted images were analyzed using the Diffusion II Toolbox implemented in SPM 8 (Statistical Parametric Mapping, version 8, Wellcome Trust Centre for Neuroimaging, London, UK; <http://www.fil.ion.ucl.ac.uk/spm/>).

The images were first corrected for head movements and eddy currents using rigid-body realignment and full affine co-registration to the b_0 -image. To allow for accurate localization of white matter tracts, the high-resolution T_1 -weighted anatomical scan of each participant was normalized to the Montreal Neurological Institute (MNI) T_1 -template. Each participant's diffusion weighted images were then co-registered to the high-resolution anatomical scan and transformed to the MNI template space using the parameters obtained from the normalization of the high-resolution anatomical scan. Images were resampled to 2 mm^3 isotropic voxels. After all registration steps were completed, the diffusion gradients were reoriented according to the realignment and normalization parameters.

The diffusion tensor was computed by entering the gradient directions and strengths into a multiple regression model. Diffusion indices Fractional Anisotropy (FA) and Mean Diffusivity (MD) were then computed from the tensor. FA is computed by equation 6.1 (see Le Bihan et al., 2001) and represents the orientation coherence of the diffusion of water protons within a voxel. FA is widely used as a measure of white matter integrity.

$$FA = \frac{\sqrt{3((\lambda_1 - MD)^2 + (\lambda_2 - MD)^2 + (\lambda_3 - MD)^2)}}{\sqrt{2(\lambda_1^2 + \lambda_2^2 + \lambda_3^2)}} \quad (6.1)$$

Linear regression analysis was employed to assess potential correlations between FA and behavioral parameters obtained from the grammatical judgement task. In this analysis, only voxels within the brain's white matter were considered. Explore DTI software (Leemans, Jeurissen, Sijbers, & Jones, 2009) was used to compute FEFA maps where FA is color-coded for the principal diffusion direction, thus allowing for localization on the correlation results in the correct white matter tract. Visualization of diffusion ellipsoids (showing diffusion strength in all directions as well as the principal diffusion direction) on the FEFA maps was also done in ExploreDTI.

6.3 Results

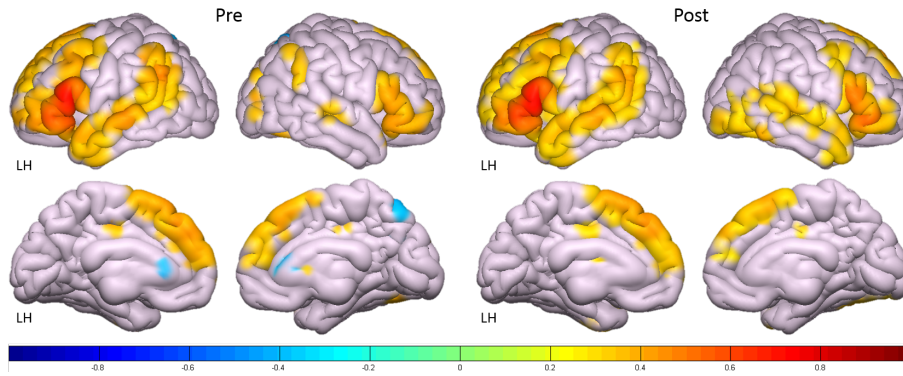


Figure 6.1: Functional connectivity of Broca's area pre and post exposure to an artificial grammar Significant ROI-to-voxel correlations at cluster-level $p < 0.05$ FWE-correction. IFG Pars Triangularis is used as an ROI to represent Broca's area. Broca's area is functionally connected to other regions in the left and right Inferior Frontal Gyri, the left and parts of the right Superior Temporal Gyri and Angular Gyri. The pre and post exposure networks did not differ significantly.

6.3.1 Behavioral results

The regression analyses conducted in the present study used behavioral parameters from an artificial grammar learning (AGL) task as covariates in order to gain insight into the relation between artificial grammar learning and Resting state functional connectivity and structural connectivity measures.

The AGL task which was used to obtain artificial grammar learning measures is described in detail in Chapter 5. Although participants were generally not able to fully acquire the artificial grammar, results showed large inter-subject variability in the success with which they gave grammatical judgments on grammatical and ungrammatical stimuli after auditory exposure to the artificial grammar (% correct responses, mean (sd): 48% (13%)). They were also better able to correctly reject violations of the grammar than to accept grammatical stimuli (two-tailed paired t-test: $T = -3.1$, $p = 0.005$).

6.3.2 Functional connectivity

Both before and after auditory exposure to the artificial grammar, a reliable functional connectivity was observed between Broca's area (seed ROI: LH Tri) and other areas involved in language processing Figure (6.1). Paired t-tests comparing the pre- and post-exposure networks did not show any significant differences.

Cond	MNI coördinates			Vox.	L/R	Brain region
	x	y	z			
Pre	-56	22	18	2164	L	Inferior Frontal Gyrus
	-54	-56	28	693	L	Supramarginal / Ang Gyrus
	-42	10	46	573	L	Premotor cortex / DFC
	-52	10	-20	293	L	MTG / Temporal Pole
	-64	-30	-2	521	L	STG / MTG
	58	22	0	694	R	Inferior Frontal Gyrus
	50	-18	-8	151	R	STG / MTG
	0	44	40	1650	L/R	Medial Frontal Cortex
	-4	48	16	246	L/R	An PFC / DLPFC
Post	-56	20	16	7262	L	Inferior Frontal Gyrus STG / MTG / Temp. Pole Supramarginal / Ang Gyrus PMC / An PFC / DLPFC / DFC Insula
	-12	16	64	3680	L/R	Medial Frontal Cortex
	50	32	-8	1918	R	IFG / PMC / DLPFC
	48	-34	2	720	R	STG / MTG
	52	10	-28	73	R	MTG / Temporal Pole

Table 6.1: Functional connectivity of Tri in Broca’s area prior to and following auditory exposure to an artificial grammar Values are FWE-corrected with a < 0.0001 threshold, resulting in a minimum cluster extent of 84 voxels and a minimum T-value of 3.88. Cond = Session pre or post exposure to an artificial grammar, L/R = Left/Right hemisphere, Vox. = cluster extent in voxels, Ang. = Angular, DFC = Dorsal Frontal Cortex, MTG = Middle Temporal Gyrus, STG = Superior Temporal Gyrus, (An) PFC = (Anterior) Prefrontal Cortex, DLPFC = Dorsolateral Prefrontal Cortex, PMC = Premotor Cortex, IFG = Inferior Frontal Gyrus

Brain region	BA	L/R	MNI coördinates			<i>p</i> -value	Vox.
			x	y	z		
Supramarginal Gyrus	40	L	-56	-52	38	0.047	22
Post. Cingulate Cortex	30,23	L	-8	-64	4	< 0.001	49
Post. Cingulate Cortex	31	R	8	-66	22	< 0.001	58
Sup. Temp / Prim. Aud.	41,42,22	L	-60	-28	8	0.003	37
Sup. Temporal Gyrus	22	R	50	-24	0	0.031	24

Table 6.2: Regions of which the functional connectivity with Tri correlated with artificial grammar learning Values are FWE-corrected with a $p < 0.05$ threshold (cluster extents > 22 voxels). BA = Brodmann area, L/R = Left/Right hemisphere, Vox. = cluster extent in voxels, Post. = posterior, Sup. = superior, Temp = Temporal, Prim. Aud. = Primary Auditory Cortex.

In order to assess the role of functional connectivity within the language network in artificial grammar learning, we tested for potential correlations between individual differences in artificial grammar learning and functional connectivity within the network found to be functionally connected to Broca’s

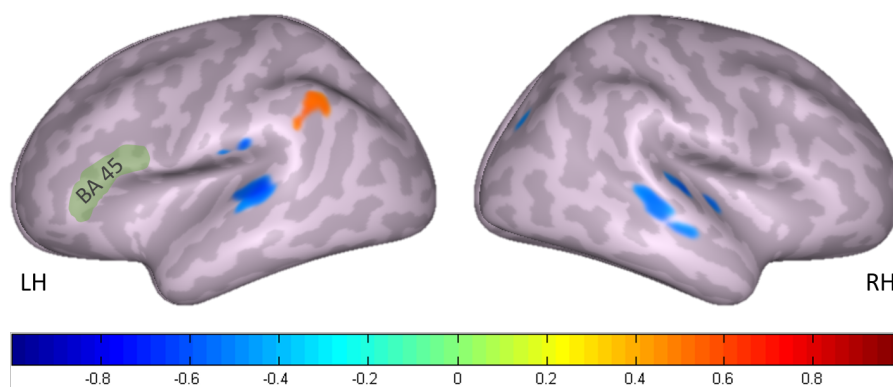


Figure 6.2: Area's where functional connectivity of Broca's area correlates with artificial grammar learning success after exposure Correlation map shows significant correlations at cluster-level with $p < 0.05$ FWE-correction. IFG Pars Triangularis (BA 45, shown in green) is used as a seed ROI in Broca's area. The left Supramarginal Gyrus (BA 40) shows a correlation with positive functional connectivity, while the bilateral superior temporal gyri show a correlation with negative functional connectivity. Hemispheres are inflated to show the negative correlation in the right Insula and Superior Temporal Sulcus

area prior to and following auditory exposure to an artificial grammar. Because earlier results showed that individual differences in the ability to reject violations after exposure to an artificial grammar correlate with brain activation during exposure (see Chapter 5), we used linear regression to test for correlations between this parameter of artificial grammar learning and functional connectivity. Our results showed that following, but not prior to auditory exposure to an artificial grammar, functional connectivity between Pars Triangularis and a cluster in the left Supramarginal Gyrus (22 voxels, $p = 0.047$) correlated with the artificial grammar learning performance of participants. Furthermore, negative correlations between artificial grammar learning and functional connectivity were found in the bilateral Posterior Cingulate Cortex (Left: 58 voxels, $p < 0.001$; Right: 49 voxels, $p < 0.001$), and in two clusters covering part of the left Primary Auditory Cortex and Superior Temporal Gyrus (37 voxels, $p = 0.003$; 24 voxels, $p = 0.031$).

A comparison of the correlation maps (Figure 6.2) shows that both the Supramarginal Gyrus cluster and the STG clusters are part of the network that is functionally connected with Broca's area on the group level both before and after auditory exposure to an artificial grammar. Therefore, the negative correlation in the bilateral STG cluster reflects less but present functional connectivity between IFG and STG in more successful learners of the artificial grammar.

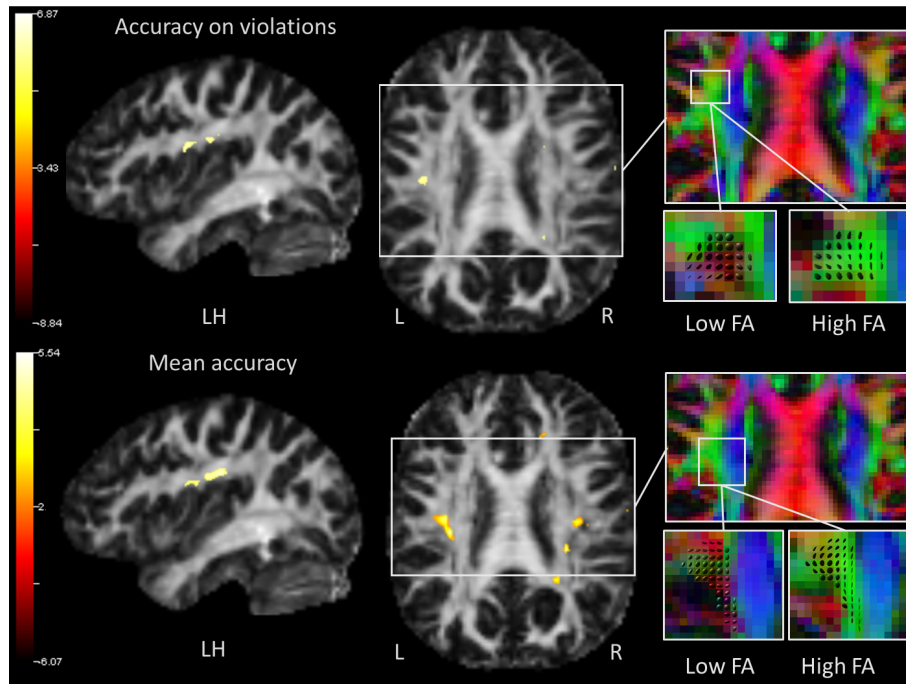


Figure 6.3: Correlation between artificial grammar learning and white matter integrity in the Arcuate Fasciculus Sagittal and Axial FA maps with correlation clusters are shown on the left and FEFA maps with diffusion ellipsoids for participants showing high and low FA's in the correlation clusters are shown on the right. Color-code principal diffusion direction: green = anterior-posterior, blue = dorsal-ventral, red = left-right. Top: Correlation between accuracy on violations and FA. Bottom: Correlation between mean accuracy and FA.

6.3.3 Structural connectivity

Linear regression analyses using both the accuracy on violations and mean accuracy on the grammatical judgement task as regressors showed correlations between fractional anisotropy in the Arcuate Fasciculus and both measures of artificial grammar learning.

In order to confirm the localization of the correlations within the Arcuate Fasciculus, clusters where a correlation with either mean accuracy or accuracy on violations was found were overlaid on an FA map which was then visually compared with the FEFA map which is color-coded for main diffusion direction. A comparison between these maps and a Diffusion Tensor Imaging atlas (Catani & Thiebaut de Schotten, 2008) showed that the correlation clusters were located in the fronto-parietal and temporal portions of the Arcuate Fasciculus.

The success with which participants rejected violations after exposure to an artificial grammar correlated with FA in the fronto-parietal portion of the

left Arcuate Fasciculus and ($p = 0.002$, FWE-corrected for whole-brain white matter: Figure 6.3 and Table 6.3). Furthermore, FA in the bilateral frontoparietal and right temporal Arcuate Fasciculus correlated with the mean accuracy on grammaticality judgements made on grammatical stimuli and violations together (Left: $p < 0.001$; Right: $p < 0.001$, FWE-corrected for whole-brain white matter: Figure 6.3 and Table 6.3). In order to test for group differences, an independent samples t-test was conducted on two groups selected based on a median split on artificial grammar learning scores. This analysis showed no significant differences (Left Occipital-Frontal Fasciculus, MNI coordinates -34 -44 0: $T_{\max} = 5.37$, $p = 0.063$). Mean diffusivity (MD) was not found to be correlated with any of the behavioral measures.

Although no correlation was found between age and any of the behavioral parameters of artificial grammar learning, previous research has shown a decline in white matter integrity with age (for a review, see Moseley, 2002). A regression analysis testing for the possible negative correlation between age and FA only revealed a correlation in the left Frontal-Occipital Fasciculus (MNI coordinates: -32 -40 14, $R^2_{\max} = 0.60$, $p = 0.042$, FWE-corrected for white matter). No negative correlation of age with MD was found within the brain's white matter. This suggests that the relation between individual differences in artificial grammar learning and white-matter integrity is not driven by age-related differences in FA.

6.4 Discussion

The present study aimed to investigate how individual differences in artificial grammar learning capacity are related to functional and structural connectivity in the healthy adult brain. Individual differences in artificial grammar learning were shown to be reflected in both functional connectivity of the frontal part of Broca's area, to other regions within the language network and white matter integrity in the Arcuate Fasciculus (AF).

Measure	AF section	L/R	MNI coordinates			FA	T_{\max}	R^2_{\max}
			x	y	z			
Viol. acc	Front-Par	L	-40	-14	24	0.65	4.67	0.55
Mean acc	Front-Par	L	-34	-22	-24	0.71	6.82	0.72
		R	40	-22	-28	0.66	5.02	0.58
	Temp	R	36	-30	2	0.80	6.16	0.68

Table 6.3: Clusters with a correlation between FA and artificial grammar learning AF section = section of the Arcuate Fasciculus where the cluster is located, L/R = Left/Right hemisphere, FA = mean Fractional Anisotropy in given cluster, Vox. = cluster extent in voxels, Front-Par = Fronto-Parietal, Temp = Temporal.

6.4.1 AGL influences resting-state functional connectivity

Resting-state functional connectivity measurements showed a similar network of brain regions that were functionally connected with IFG Pars Triangularis (Tri), the frontal part of Broca's area before and after auditory exposure to a new artificial grammar. Although AGL did not show a significant effect on the network connected with Tri, behavioral parameters of artificial grammar learning were correlated with functional connectivity after, but not prior to exposure to the grammar. Specifically, after AGL a correlation was found between artificial grammar learning success and functional connectivity between Tri and the Supramarginal Gyrus (SMG). Furthermore, a negative correlation was found between AGL success and functional connectivity between Tri and the bilateral posterior Superior Temporal Gyrus (STG) and Superior Temporal Sulcus (STS). This finding suggests that functional connectivity within the language network is influenced by auditory exposure to an artificial grammar.

The network of brain regions found to be functionally connected to Broca's area after AGL exposure is largely consistent with functional connectivity of Broca's area reviewed in (Tomasi & Volkow, 2012) and fMRI results reported in (C. J. Price, 2010) and includes the bilateral posterior STG and STS. Therefore, the negative correlation between functional connectivity of Broca's area with bilateral STG and STS and AGL success should be interpreted as a lower, not negative, functional connectivity in more successful learners compared to less successful learners after exposure to an artificial grammar. While showing lower functional connectivity between Broca's area and bilateral STG/STS, these participants showed higher functional connectivity between Tri and the Supramarginal Gyrus. This suggests that a relatively strong functional connectivity between Tri area and SMG combined with a weaker FC between Tri and posterior STG might enable participants to learn a grammar more successfully or, alternatively, might be induced by successful artificial grammar learning.

Bilateral posterior STG/STS have been implicated in phonological processes of speech recognition (e.g. Hickok, 2009) and semantic processing (Friederici, Rueschemeyer, Hahne, & Fiebach, 2003). Furthermore, the SMG cluster is adjacent to Wernicke's area and is consistent with the SMG cluster that was found to be functionally connected with Broca's area in a meta-analysis of RS-fMRI data from a large sample of healthy participants (Tomasi & Volkow, 2012). Furthermore, SMG was previously shown to be functionally connected to IFG during speech processing tasks with high processing loads when stimuli were predictable (Obleser, Wise, Dresner, & Scott, 2007). Because the current experiment was conducted under difficult listening conditions and stimuli were more predictable for more successful learners, this might explain the correlation between functional connectivity and artificial grammar learning. Our data suggest that a higher functional connectivity between IFG Pars Triangularis and SMG through the anterior part of the dorsal language path-

way (Hickok & Poeppel, 2004; Parker et al., 2005; Rauschecker & Scott, 2009) aids syntactic processing.

6.4.2 Contribution of the dorsal language pathway to AGL

Individual differences in artificial grammar learning capacities were not only related to functional, but also to structural connectivity measures. Our results showed correlations between Fractional Anisotropy in the fronto-parietal section of left Arcuate Fasciculus and the success with which participants rejected violations of a learned artificial grammar, while response accuracy on both grammatical and ungrammatical stimuli correlated with FA in the bilateral fronto-parietal Arcuate Fasciculus.

The Arcuate Fasciculus connects the IFG, Middle Frontal Gyrus and Precentral Gyrus with the Superior and Middle Temporal Lobes and the Supramarginal Gyrus (e.g. Catani & Thiebaut de Schotten, 2008; Parker et al., 2005) and has since long been established as an important connection in the language network (Geschwind, 1965). Together with the Superior Longitudinal Fasciculus, the Arcuate Fasciculus forms the anatomical basis for the dorsal language pathway (Hickok & Poeppel, 2004; Saur et al., 2008). Decreased FA in the Arcuate Fasciculus has been shown to play a role in speech and language deficits like stuttering (Chang, Erickson, Ambrose, Hasegawa-Johnson, & Ludlow, 2008) and Specific Language Impairment (Vallée et al., 2014).

The finding that participants who performed better when learning an artificial grammar showed a higher FA in the Arcuate Fasciculus, suggests that the AF and the dorsal language pathway contribute to syntactic processing and language learning. This is in accordance with previous studies showing that white matter integrity in the left (Flöel et al., 2009; Lopez-Barroso et al., 2011) and right (Loui, Li, & Schlaug, 2011) hemisphere can predict different aspects of artificial grammar learning and second language learning (Li, Legault, & Litcofsky, 2014) success.

Purely based on the results of the current study, it cannot be determined whether the presence of more coherent white matter in AF leads to better grammar learning capacities, whether increased grammar learning experience and ability leads to higher FA in the Arcuate Fasciculus through a "use-it-or-lose-it"-effect or whether a third factor drives both. FA can reflect both macro-structural (fiber orientation coherence) and micro-structural (myelination) attributes of white matter and myelination has been suggested as a source of adult plasticity because it extends into adulthood and has been associated with activity-driven plasticity (Fields, 2005). Therefore, increased FA in the Arcuate Fasciculus can be both a cause and an effect of higher (artificial) grammar learning capacity. Further studies addressing the development of individual differences in grammar learning ability will be needed to shed light on this issue.

6.4.3 Conclusion

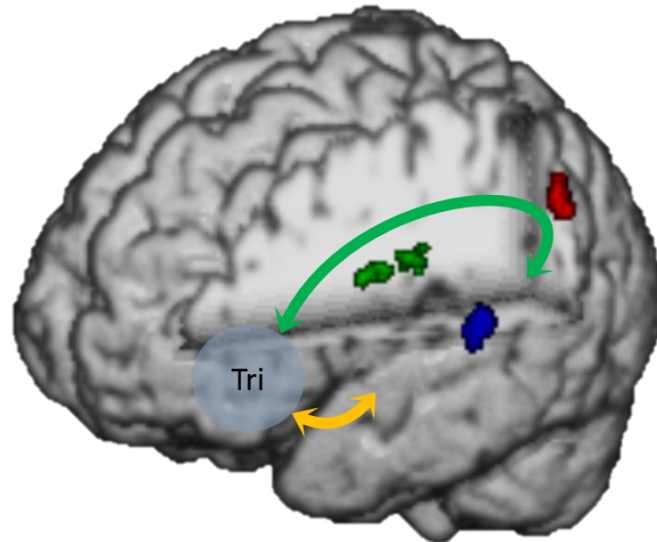


Figure 6.4: Ventral and dorsal language pathways in relation to the correlations found between functional connectivity and AGL. Correlation between accuracy on violations and FA in the left Arcuate Fasciculus (green cluster) and positive (red cluster) and negative (blue cluster) correlations between accuracy on violations and FC with Tri. Pathways: green = Dorsal Pathway, yellow = Ventral Pathway. The dorsal pathway runs through the Arcuate Fasciculus and the Superior Longitudinal Fasciculus and the ventral pathway runs through the Extreme Capsule

An integrated analysis of functional and structural connectivity within participants might allow for a better understanding of the underlying mechanisms leading to individual differences in artificial and possibly natural grammar learning. Figure 6.4 summarizes the correlations found between behavior and both functional and structural connectivity. Prior research has shown that artificial grammar learning in older adults is linked to functional and structural connectivity (Antonenko, Meinzer, Lindenberg, Witte, & Flöel, 2012). The present study revealed both a higher FA in the anterior part of the Arcuate Fasciculus, and a higher functional connectivity between Pars Triangularis and the Supramarginal Gyrus in participants who performed better on an artificial grammar learning task. These results suggest that increased connectivity between Tri and SMG through the dorsal language pathway, specifically the Arcuate Fasciculus, is beneficial to artificial grammar learning and might thus play a role in syntactic processing.

It is conceivable that a higher white matter integrity or myelination of AF in more successful learners also allows for increased functional connectivity in these participants. Although the correlation between functional connectivity and artificial grammar learning measures was only found after auditory

exposure to and artificial grammar, it is unlikely that this correlation is purely task-related, because the structural connectivity data show a similar effect. A possible explanation is that successful learners possess a language network with stronger white matter connections, within which important connections are engaged when they are faced with the task of acquiring an artificial grammar. In learners who have more difficulties learning the grammar, the structural connectivity between Tri and SMG might be weaker, allowing for less functional connectivity between these regions.

