Specialization of phonological and semantic reading routes in early childhood

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Abstract

Children show dramatic changes in their reading ability as they are taught to read. During the early period of development, they gain phonological (letter to sound mapping) and semantic knowledge (storage and retrieval of word meaning) of language. This study aims to identify the specialization of phonological and semantic reading routes in early childhood using a combination of univariate and multivariate pattern analysis. 19 typically developing children, between the age of five to seven, performed visual word-level, phonological (rhyming), and semantic (related meaning) judgment fMRI tasks. Using multivariate analysis, we provide the first evidence that young children with good reading ability, have already established specialization in left-hemisphere regions for the two reading routes, including the inferior frontal gyrus (IFG), superior and mid temporal gyrus (STG/MTG) and fusiform gyrus. Additionally, semantic information retrieval relies on bilateral inferior parietal lobe areas. The results of the multivariate analysis also provide evidence for the specialization of frontal sub-regions, IFG opercularis, for phonological processing. However, our study does not show evidence for temporal specialization for phonological processing and fronto-temporal specialization for semantic processing. Our findings provide evidence for specialization in the brain, supporting the dual-route theory for reading in early childhood for typically developing children, which can be used as a control baseline for comparison of children at-risk for reading difficulties.

1 Introduction

In the present society, learning to read as a child is the foremost step to develop high literacy skills. Teaching a child to read begins at birth with the reinforcement of pre-literacy skills, and most children officially learn to read between the ages of 5 and 7. Teaching a child to read usually happens by two methods, sounding-out method and sight-word reading. One of the most common ways to learn to read is via the sounding-out method in which children are encouraged to read aloud, pronouncing each letter or group of letters to recognize the word by sound. Simultaneously, children are taught sight words or common vocabulary that they can memorize to reduce the cognitive burden of decoding sentences. Thus, word reading can be achieved through two distinct mechanisms, grapho-phonological processing (letter to sound correspondence) and lexico-semantic processing (direct mapping of words to meaning). The grapho-phonological processing requires words to be transformed into their auditory counterparts through a grapheme to phoneme correspondence and then to its meaning. On the contrary, the lexico-semantic processing corresponds to a direct association between the visual form of the word to its meaning. The specialization of the neural pathways for reading is well established in adults (Coltheart et al. 2001; Jobard et al. 2003; Vigneau et al. 2011). However, it remains unclear if the reading pathways are specialized in early childhood for children within 5 to 7 years of age. The understanding of reading pathways is not only crucial for theoretical models of cognitive development, but also for understanding how children with reading impairment deviate from the typical trajectory.

The dual-route theory suggests that different neural pathways are associated with the two reading mechanisms (Hickok and Poeppel 2007; Price 2012; Friederici and Gierhan 2013). A systematic meta-analysis has laid an objective picture of the dual-route of the reading framework in adults (Jobard et al., 2003). The grapho-phonological processing relies on left-lateralized brain structures, including the superior temporal gyrus (STG), dorsal inferior parietal lobe (IPL: supramarginal gyrus and angular gyrus), and the opercular part of the inferior frontal gyrus (IFG), the last two regions reflect a more significant load in working memory during phonological access. The lexicosemantic processing is thought to arise from the co-activation of the fusiform gyrus (visual word form area, VWFA), basal inferior temporal area, the posterior part of the middle temporal gyrus (MTG), and the orbitalis part of IFG. The triangularis part of IFG has

been suggested to be recruited in both the phonological as well as the semantic route of reading (Jobard et al., 2003).

A few studies have investigated the reading pathways in children using visual word-level reading tasks (Bitan et al. 2006; Cao et al. 2006, 2008; Hoeft et al. 2006, 2007; Bitan, Burman, et al. 2007; Bitan, Cheon, et al. 2007; Li et al. 2018). However, all these studies have accounted for reading mechanisms in children during late childhood, that is, 8-15 years of age. Recent literature has suggested that the atypical brain structure and functions are present in children at-risk for developmental dyslexia in early childhood, 5-7 years of age (Raschle, Zuk, and Gaab 2012; Im et al. 2016; Wang et al. 2016; Yu et al. 2018) and even as early as in infancy (Langer et al. 2015; Sideridis et al. 2019). Thus, understanding the "reading" network in the brain during early childhood will help us understand the neural mechanism of reading development during this crucial early period, which may help identify at-risk children for delayed reading and language achievement later and provide early intervention during early childhood.

Past studies have implemented phonological and semantic decision tasks to understand the double dissociation of the dual-route theory. While performing the phonological decision tasks, like rhyme judgment, children have to access the sounds of the words and are therefore more likely to engage the indirect route. Using English rhyming words for phonological decision, activation has been localized to bilateral brain areas including the fusiform gyrus, STG/MTG, SPL, precentral gyrus, IFG and SFG/MFG (Hoeft et al., 2006; Hoeft et al., 2007; Cao et al., 2006; Cao et al., 2008; Bitan et al., 2007a). The visual word-level semantic judgment tasks using English word pairs have been administered on children to identify the semantic reading route (Booth et al. 2001, 2003, 2004; Blumenfeld et al. 2006). The semantic decision task requires children to make a judgment, for instance, whether the stimulus presented is a word, or if the two words presented are related. Thus, it is requisite to access the meaning of the word, which can be achieved without access to its pronunciation. The semantic reading route in children also relies on bilateral brain areas, including the fusiform gyrus, ITG/MTG, IPL, and IFG. Thus, past research studies indicate no explicit hemispheric specialization for reading even in late childhood as both hemispheres are involved in the reading tasks.

There are a limited number of studies that have accounted for the specialization of the two reading routes by directly comparing brain activation for phonological and semantic processing in children using visual word-level reading tasks. In an fMRI study, Landi et al. (2010) directly compared the reading-related activation amongst the phonological and semantic English-word judgment tasks in a within-group design. They used a mixed stimuli presentation (orthographic and pictorial) and found greater semantic-related activation in the left STG and angular gyrus, as compared to phonological-related activation. They also reported that no brain region showed greater phonological compared to semantic-related activation. However, this study recruited adolescents in a wide age range (9 to 19 years); thus, the specialization of the semantic reading route might be biased by an age effect. On the contrary, the studies in Chinese (Cao et al. 2009; Liu et al. 2018) report no significant difference between visual phonological and semantic decision-making tasks for children within the age range of 9-12 years, suggesting the topological organization of children's reading network is not specialized. They report activation in left-lateralized brain areas, including left middle frontal gyrus (MFG), left inferior frontal gyrus (IFG), left fusiform gyrus (FG), and right middle occipital gyrus (MOG) for both semantic and phonological decision-making tasks. However, Chinese reading is different from English reading, which might contribute to the different findings (Chen et al. 2002). In summary, past research using visual reading tasks have speculated that the two reading routes are not well specialized even by late childhood.

The past studies have only relied on the univariate analysis approach to investigate the differences between the recruitment of brain areas for the two reading mechanisms. However, recent research has shown that the neural differences may be invisible to subtraction-based fMRI analysis if task differences are represented not by different levels of activity within single voxels, but by differential neural activity patterns within a region of the cortex (Haynes and Rees 2006; Norman et al. 2006). Thus, we used a relatively new mapping strategy, the searchlight analysis (Kriegeskorte et al. 2006), to explore the neuroanatomical basis of the two reading mechanisms. This technique, based on multivariate pattern-analysis (MVPA) (Haxby et al. 2001; Pereira and Botvinick 2011), probes local information of neural pattern differences across different conditions by moving a searchlight unit on a voxel-by-voxel basis. MVPA has several advantages compared to traditional, and more commonly used, univariate analyses. Primarily, MVPA can provide more sensitivity in discriminating conditions of interest than univariate

approaches because it considers patterns of voxel activity that may show weak but consistent differences between conditions (Oosterhof et al. 2016).

The objective of the present study was to understand the neural specialization of phonological and semantic processing in early childhood, 5-7 years of age. In this research study, we investigated the early specialization of reading pathways using visual reading tasks. We used visual rhyming and semantic judgment tasks to probe the specialization of the two reading routes. All words were presented with child-friendly images of the corresponding words to assist children in reading words, similar to Debska et al. (2016). Applying different criteria for a match in these tasks (either rhyming or semantic association) allowed us to measure the effects of conscious access to the two reading pathways. Based on past research conducted on older children using visual reading paradigms (Bitan et al., 2006; Bitan et al., 2007a; Bitan et al., 2007b; Cao et al., 2006; Cao et al., 2008; Hoeft et al., 2006; Hoeft et al., 2007; Li et al., 2018), we hypothesized the recruitment of bilateral frontal and temporoparietal areas for both phonological and semantic processing. We conducted multivariate pattern analysis to understand the specialization of brain areas for phonological and semantic processing. The combined use of univariate and multivariate methods can provide necessary complementary information (Poldrack and Farah 2015; Lyu et al. 2016) to improve the understanding of brain activity during phonological and semantic processing for reading in early childhood.

2 Methods

2.1 Participants

47 healthy native English-speaking children were recruited for the study. The study involved two sessions. During the session-1, children underwent a series of standardized behavioral tests. The details of these tests administered to the participants is provided in the section below. The participant's parents were asked to fill out a follow-up questionnaire about the child's developmental history. Based on the questionnaire, any participant with 1) a diagnosis of Attention Deficit Hyperactivity Disorder (ADHD), 2) hearing or vision impairment, 3) neurological or psychiatric disorders, 4) a diagnosis of language disorder or reading disability, or 5) with any contraindications to be scanned in an MRI, was excluded from the study.

The inclusion criteria for participants for the fMRI visit (session-2) were: (1) native monolingual English speakers and (2) right-handed as measured by handedness questionnaire (adapted from Oldfield, R.C. (1971). Based on the standardized test scores the inclusion criteria was, (3) non-verbal intelligence of at least a standard score of 80 (M=106.40, SD=16.51) as measured by the Kaufman Brief Intelligence Test, Second Edition (KBIT-II, Kaufman, 2004). We also conducted a computer-based 'familiarity task'. In this task, children read thirty 3-5 letter monosyllabic words and choose the corresponding picture that represents the word. Based on familiarity task scores, the final inclusion criterion was (4) accuracy greater than 70% in the familiarity task. Out of the initial 47 participants, 20 participants were recruited for the fMRI session based on the inclusion criteria mentioned above.

For one participant, whole-brain data was not acquired as observed by mask cut-off from the visual cortex due to excessive motion artifacts. Thus, this participant was excluded from fMRI data analysis. The final sample included 19 participants; all were right-handed (8M, 11F; average age 6.55 years (age range: 5 year 4 months – 7 year 9 months).

The Institutional Review Board approved all experimental procedures at the University of Nebraska at Lincoln. Written consent forms were obtained from the parents or guardians, and written assent forms were also obtained from children who were older than seven years old.

2.2 Behavioral Measures

Behavioral measures were acquired during the first visit as part of a battery of standardized tests. We measured the participants' phonological awareness, word association skills, and word reading ability. The phonological awareness was measured using the Phonological Awareness (PA) subtest of WRMT-III (WRMT-III-PA). This test measures awareness of the phonological components of language (e.g., phonemes and syllables). The test is divided into five sections: first sound matching, last sound matching, rhyme production, blending, and deletion. In the first and last sound matching, the participants are asked to point to a picture (out of the four options) that begins/ends with the same sound as the word indicated by the experimenter. In the rhyme production, the examinee is prompted to name a real or made-up word that rhymes with a given word. In blending, the examinee must combine phonemes or syllables and identify the word they create. In deletion, the examinee is prompted to say the word that is created when one phoneme

or syllable is removed from the beginning or end of the stimulus word. A standard score of PA is generated on the basis of performance in all the five sections of the subtest.

The word association skill was measured with the Word Classes sub-test from the Core Language Score in the Clinical Evaluation of Language Fundamentals test (CELF-5; Wiig, Messing Semel, & Secord, 2003). In this test, participants are asked to select two (out of three/four) words that go together. The CELF was acquired for 12 out of the 20 participants that were included in the final sample.

The word reading ability of participants was measured using the word identification subtest of WRMT-III (WRMT-III-WID). The word identification test requires an individual to read words of increasing difficulty.

2.3 fMRI Data

2.3.1 Stimuli

3-5 letters monosyllabic words suitable for young children, were selected for the experiment. The word pairs were matched on concreteness, printed familiarity, word type (noun), and the number of syllables using the MRC (Medical Research Council) psycholinguistic database (Wilson 1988). For the semantic judgment task, the association index was estimated for the word pairs (Buchanan et al. 2013). Each word pair was searched in the double word pair database (http://wordnorms.com/). Latent Semantic Analysis (LSA) was done on the chosen word pairs for the semantic association task. The LSA shows both the semantic and thematic relationships between word pairs. The average LSA value estimated for semantically related word pairs (e.g., LION -TIGER, LOCK-KEY) was 0.45 (S.D.=0.16). In the unrelated condition, the two words had zero semantic association (e.g., OWL-MAP, BOOT-KITE). For the phonological judgment task, the rhyming word pairs shared the same vowel and final phoneme/cluster corresponding to 2-3 letters at the end of its written form (e.g., CAT – BAT, TRAIN-CHAIN). For the non-rhyming condition, there were no shared phonemes or letters of its written form (e.g., ARM-BED, CLOCK-KITE).

2.3.2 fMRI Paradigms

Both rhyming and semantic judgment tasks presented word stimuli visually with a child-friendly image above the corresponding words (see Figure 1A and B). Each word was presented for a duration of 800 ms with a 200 ms gap between the presentation of the two words. After the presentation of the two words consecutively, the response screen was shown to the participants for a duration of 2200 ms. Both the words appeared simultaneously on either half of the screen with a question mark in between the two words. The participants were instructed to respond when they see the question mark on the screen. If there was a match, they pressed a button with their right hand; if there was no match, they pressed a button with their left hand. Participants were encouraged to respond as quickly as possible without making errors. In the perceptual control condition, symbol strings (non-alphabetic glyphs) were presented visually in sequential order, and then the two strings appeared simultaneously on the screen with a question mark in between. Once the question mark appeared, the participant had to determine whether the strings matched or not. Timing parameters and button press instructions were the same as for the rhyming (and semantic) task conditions. The strings comprised of 3-5 non-alphabetic glyph characters. Child-friendly images were shown with the strings, too, to control with task stimuli. In addition to the perceptual control condition, fixation trials were included as a baseline. In the fixation condition, a black fixation cross was presented and participants were instructed to press a button when the black fixation cross turned red. The total duration of the fixation trial was 10s (see Figure 1).

For the rhyming task, the child determined whether the two words with pictures, presented visually-only, consecutively, rhyme, or not. For the semantic task, the child determined whether two words with pictures, presented visually-only, consecutively, associate or not. Two runs were administered for each task to reduce the effect of fatigue, and block design was used to achieve a higher detectability of brain activation in pediatric fMRI data (Gore 2003; Wilke et al. 2003). Each run comprised of 8 blocks (4 task blocks and 4 control condition blocks) and started with a fixation block followed by the task block, then fixation and control block (see Figure 1D). Each rhyme task block consisted of 8 trials (4 rhyming/ 4 non-rhyming), and the control block consisted of 4 trials (2 matching/2 non-matching). Thus, each rhyming run consisted of 32 stimuli trials (16 rhyming/ 16 non-rhyming word pairs), 16 perceptual control trials, and 8 fixation trials. Similarly, each semantic task block consisted of 8 trials (4 semantic/ 4 non-semantic), and the control block consisted of 4 trials (2 matching/2 non-matching). Thus, each

semantic run consisted of 32 stimuli trials (16 semantically associated/ 16 not-associated word pairs), 16 perceptual control trials and 8 fixation trials.

The order of presentation of runs was counterbalanced across subjects, such that 9 participants completed rhyming runs first, whereas the other 10 completed semantic runs. The presentation of stimuli within a block (stimuli and perceptual control) was randomized within each run. In the beginning of each run, 5-sec fixation was presented, which allowed the fMRI signal to stabilize. Each run lasted for 4 min 37 sec (277 TRs). Thus, the total duration of the four runs of rhyming and semantic tasks was 18 min and 28.8 sec.

----------Insert Figure 1----------

2.3.3 fMRI data acquisition

Brain image data were acquired using a 3.0-Tesla Skyra Siemens scanner with a 64- channel head coil. The blood-oxygen-level-dependent (BOLD) signal was measured using a multiband EPI (University of Minnesota sequence cmrr_mbep2d_bold) sequence with the following parameters: TR = 1000 ms, TE = 29.80 ms, flip angle = 60 degrees, matrix size = 210 x 210 mm^2, field of view = 210 mm, slice thickness = 2.5 mm, number of slices = 51. Voxel size = $2.5\times2.5\times2.5mm^3$. Before functional image acquisition, a high resolution T1-weighted 3D structural image was acquired for each subject using a multi-echo magnetization prepared rapid gradient echo (MPRAGE) sequence (TR = 2530 ms, TE1 = 1.69 ms, TE2 = 3.55 ms, TE3 = 5.41 ms, TE4 = 7.27 ms, matrix size = 256×256 mm^2, field of view = 256 mm, slice thickness = 1 mm, number of slices = 176, TA = 6.03 minutes).

Before the actual imaging session, each child went through half-an-hour practice training in a child-friendly “MRI-like” room (a mock scanner room equipped with a nonmagnetic MRI simulator, Psychology Software Tools, Model#100355). Literature has suggested that pre-training session is crucial for young children and increases the success rate, as well as reduce the motion artifacts and anxiety (Leach and Holland 2010; Raschle, Zuk, Ortiz-Mantilla, et al. 2012). For this study, we achieved a 95% success rate through the use of a mock session. During the mock session, participants were exposed to different scanner noise and practiced the experimental tasks until they achieved accuracy above 60%. The practice version of the experimental tasks used different words to avoid overlapping with actual stimuli.

Participants were positioned in the MRI scanner with their head secured using foam pads. A two-button response pad was placed in the participant's left and right hand to log responses. Head motions were controlled using elastic straps that were attached to either side of the head-coil apparatus. Additionally, participants wore OptoActive™ active noise canceling headphones (OptoAcoustics, Mazor, Israel, http://www.optoacoustics.com/medical/optoactive/features) to minimize the effects of the ambient scanner noise.

2.4 fMRI Data Analysis

2.4.1 Univariate Analysis

Standard preprocessing steps were performed in SPM12 (Wellcome Department of Cognitive Neurology, London, https://www.fil.ion.ucl.ac.uk/spm/). Re-alignment and ArtRepair (Mazaika et al. 2007) process were used to correct for head motions. The parameters for Art-Repair outlier detections were: global mean signal change z = ± 9 and exceeding 4 mm of head motion. Outliers and volumes with excessive motion identified by ArtRepair were de-weighted in the GLM analysis. Structural images were segmented and normalized to the segmented pediatric template NIHPD (4.5-8.5 years) obtained from the Neuroimaging and Surgical Technologies Lab, MNI, Canada, http://nist.mni.mcgill.ca/, (Fonov et al. 2011). The template is based on brain imaging data from 82 healthy young children. Then, functional images were coregistered to structural images accordingly. Finally, fMRI data were smoothed using an 8x8x8 mm^3 isotropic Gaussian kernel.

Four conditions — Fixation, Rhyming, Semantic, and Control were modeled using the GLM framework. Each of the four runs was modeled in a separate GLM. The head motion and outlier were regressed out in the GLM analysis. A high-pass filter with a cutoff of 128s and an artificial mask threshold of 0.2 were applied. Whole-brain statistical parametric mappings were generated, and contrasts were then defined to reveal brain areas specifically involved in the phonological processing (Rhyming > Control) and semantic processing (Semantic > Control). The individual statistical maps were further entered into a group-level random-effects analysis, and the significant clusters were identified at a cluster threshold $k > 20$, FDR corrected ($q < 0.05$).

2.4.2 Multivariate Pattern Analysis

MVPA (Haxby et al. 2001) is based on comparing spatial patterns of activation in response to different experimental conditions rather than contrasting the amplitude of the BOLD response in individual voxels as in univariate analysis (Connolly et al. 2012; Haxby 2012). While the univariate analysis reveals brain areas that show significantly different activation strengths under different conditions, MVPA identifies the differences between brain activity patterns even when the activation strengths are comparable (Norman et al. 2006; Mur et al. 2009).

Specifically, we employed a whole-brain searchlight analysis, a recently developed MVPA technique for identifying locally informative areas of the brain (Kriegeskorte et al. 2006) that may outperform mass-univariate analyses due to its higher sensitivity to distributed coding of information (Mur et al. 2009; Jimura and Poldrack 2012; Davis et al. 2014). We performed searchlight analysis using a linear discriminant analysis (LDA) classifier implemented in CoSMoMVPA toolbox (Oosterhof et al. 2016). Two separate searchlight analyses were conducted to examine the spatial pattern of voxels in the brain that the classifier could reliably (i.e., significantly above chance) distinguish between (1) rhyme processing from control task, and (2) semantic processing from control task. The SPM maps (con images) for the main effects of experimental conditions for each block in a run were stacked together and submitted to the searchlight analysis across the entire brain using 100 voxel searchlight spheres. Classification accuracies were obtained using a leave-one-out cross-validation method with an 8-fold partitioning scheme for each subject. For each of the four runs, the dataset was split into eight chunks (each corresponding to one experimental block), and the classifier was trained on the data from seven chunks and tested on the remaining one. The procedure was repeated for eight iterations, using all possible train/test partitions, and the average decoding accuracies across these iterations were calculated.

At the group level, we performed a two-tailed one-sample t-test across individual maps where classification was significantly above chance (50%, since our classifiers were binary). The resulting statistical maps were corrected for multiple comparisons using a cluster-based Monte Carlo simulation algorithm implemented in the COSMOMVPA toolbox (Oosterhof et al., 2016, clusterstat maxsum function with 1000 Monte Carlo simulatio) (corrected cluster threshold $\alpha = .01$, two-tailed; $z > 1.96$).

3 Results

3.1 Behavioral Analysis Results

The 19 participants that were included in the final sample performed average on the phonological awareness test (average standard score=113.16, SD=13.85), and had average reading ability (average standard score= 112.76, SD=14.41). The CELF was acquired for 12 out of the 19 participants that were included in the final sample. The participants performed above average on the CELF word association test (mean scaled score= 12.83, SD=2.37).

The in-scanner performance data of accuracy and reaction time (RT) (for correct responses) are provided in Figure 2 and Table 1 for both rhyming and semantic judgment tasks. Children performed better in control tasks as compared to reading tasks (refer to Figure 2 and Table 1). A paired sample t-test revealed that the accuracy of control task was significantly higher than the rhyming task ($t(18) = -3.23$, $p<.05$) and the semantic task ($t(18) = -3.52$, $p<.05$). Furthermore, the reaction time of control task was significantly lower than the rhyming task ($t(18) = 3.24$, $p<.05$) and the semantic task ($t(18) = 2.91$, $p<.05$). Besides, there were no significant differences in accuracy and RT between the rhyme and semantic judgment blocks.

----------Insert Figure 2, Table 1----------

3.2 Univariate analysis of fMRI Data

The univariate voxel-wise results of each task within the whole-brain anatomical mask are shown in Figure 3 and regions activated are reported in Table 2 and Table 3. The univariate voxel-wise contrasts at a corrected threshold of FDR, $q < 0.05$ with a cluster size greater than 20. The results of rhyme versus control indicated significant activations in the left frontal cortex, including the left inferior frontal gyrus, IFG (p. triangularis, p. opercularis and p. orbitalis), left precentral gyrus and left supplementary motor area, SMA (see Figure 3A and Table 2). A significant activation was also observed in left occipital-temporal junction encompassing the fusiform gyrus. At an uncorrected threshold, $p < 0.01$, cluster threshold greater than 20 voxels activity was also observed in bilateral superior and mid temporal (STG/MTG) cluster, bilateral

prefrontal cortex, alongwith right IFG (p. triangularis) and right pre/post central gyrus. (see supplementary Figure 1 and Table 2). The results of semantic versus control show significant activations in the left IFG. The activation cluster extends from left IFG (p. triangularis, p. opercularis and p. orbitalis), to the left mid frontal gyrus (MFG), left precentral gyrus, left SMA and right IFG (p. triangularis and p. orbitalis). A significant bilateral temporal cortex activity was also observed in MTG/ITG and fusiform gyrus (see Figure 3B and Table 3).

The direct task comparison within the whole-brain mask showed no significant difference between the rhyme judgment task as compared to the semantic judgment task. There was no significant cluster for the opposite contrast either.

----------Insert Figure 3, Table 2 and Table 3----------

3.3 Multivariate analysis of fMRI data

In the whole-brain searchlight MVPA, voxel-wise linear LDA classifiers were trained for the following condition pairs: (1) rhyme versus control and (2) semantic versus control to identify areas that can reliably distinguish the phonological and semantic processing, respectively.

For rhyme versus control searchlight analysis, significant decoding accuracy was observed in left fronto-temporal areas, including the left STG/MTG cluster, left IFG opercularis and precentral gyrus (see Figure 4A, Table 4). For semantic versus control searchlight analysis, significant decoding accuracy was observed in left fronto-temporal and bilateral parietal areas. Amongst temporal areas, a cluster extending from left STG/MTG to fusiform gyrus significantly decoded semantic from control condition. The temporal cluster also extends to bilateral parietal areas (precuneus, supramarginal gyrus, angular gyrus and IPL). Amongst frontal areas left IFG orbitalis cluster extending to left IFG (p. triangularis and p. opercularis), left MFG and precentral gyrus, decoded semantic task significantly above chance. (see Figure 4B, Table 5).

----------Insert Figure 4, Table 4 and Table 5----------

4 Discussion and Conclusion

While performing the phonological judgment tasks, children have to access the sounds of the words and are therefore more likely to engage the grapho-phonological reading route (Hoeft et al., 2006; Hoeft et al., 2007; Cao et al., 2006; Cao et al., 2008; Bitan et al., 2007a). The semantic decision tasks require them to decide if the two words presented are related, and thus they are more likely to engage the lexico-semantic reading route (Blumenfeld et al., 2006; Booth et al., 2001; Booth et al., 2003; Booth et al., 2004). In this study, we examined the early specialization of reading using visual rhyming and word-association tasks during fMRI in young children, age range from 5-7 years. While our univariate results indicate bilateral activation pattern, the MVPA results reveal a left hemispheric specialization. Our study provides evidence that young children with good reading ability, have already established the grapho-phonological reading route in the brain to support early stages of reading, including left fusiform gyrus, STG/MTG and IFG. In addition, our results indicate that the lexico-semantic processing relies on not only the left hemisphere areas including the fusiform gyrus, STG/MTG and IFG, but also the bilateral parietal areas covering IPL. The MVPA results give a detailed account of specialization of fronto-temporal sub-regions for phonological and semantic processing. Specifically, the MVPA results suggest that IFG opercularis is specialized for phonological processing but none of the IFG sub-regions are specialized for semantic processing. Additionally, no temporal specialization is observed for phonological or semantic processing. We discuss these findings in detail below.

4.1 Left Hemispheric Specialization for reading in early childhood

Our univariate results agree with previous research (Bitan et al., 2006; Bitan et al., 2007a; Bitan et al., 2007b; Cao et al., 2006; Cao et al., 2008; Hoeft et al., 2006; Hoeft et al., 2007; Li et al., 2018), that report bilateral frontotemporal involvement for both phonological and semantic processing. However, the multivariate results indicate specialization of phonological and

semantic processing to left-hemisphere fronto-temporal areas. Significant multivariate decoding of rhyme as compared to control condition was localized to the left hemisphere, in the left fusiform gyrus, left STG/MTG, left IFG, and precentral gyrus (refer to Figure 4A and Table 4). Also, significant multivariate decoding of semantic as compared to control condition was localized to the left hemisphere, in the left fusiform gyrus, left STG/MTG, left IFG, and precentral gyrus (refer to Figure 4B and Table 5). Our MVPA results suggest hemispheric specialization of reading to the left frontotemporal areas and fusiform gyrus occurs in early childhood. The left hemispheric lateralization for reading has been reported to be related to children's reading ability in early childhood (Yamada et al., 2011). Yamada et al. used a one-back letter reading task on five-year-old children who received reading instruction in kindergarten, and showed that typically developing children with on-track pre-literacy skills recruited left-lateralized temporoparietal regions. In contrast, children at risk of reading difficulty showed bilateral activation. The hemispheric lateralization observed in our study could result from the good pre-reading skills of our sample. In total, 60 children completed the first behavioral testing session, but only 20 out of 60 children were invited back to the second fMRI session (33%) based on their pre-reading skills, which biased our sample. The 20 children recruited for the fMRI session were good readers, as indicated by their average scores on behavioral reading tests (WRMT and CELF) and a greater than 70% in-scanner task accuracy. This is the limitation of the current study. Since we were interested in the specific functional processes in the brain, it was hard to include all the children with various levels of pre-reading skills across age groups. We could have used lower-level cognitive tasks such as first-sound matching (Raschle, Zuk, and Gaab 2012; Raschle et al. 2014; Yu et al. 2018) or letter identification (Yamada et al. 2011), but it would have been too simple for those who were seven years old. We also collected resting-state data for the group children recruited for fMRI session, but the limitation of resting-state data is that it does not give information about the specific cognitive processes of interest. Although we could identify some characteristics of resting-state networks for all children at various levels of pre-reading abilities, the neural mechanism of relating resting-state networks to another cognitive process is unclear and troublesome. For future research, age-appropriate cognitive paradigms are needed to pinpoint the pre-reading processes in the brain.

4.2 Specialization of brain regions for phonological and semantic processing

4.2.1 Fronto-temporal lobe

Studies that have directly compared phonological and semantic related activation in adults found a double-dissociation between the tasks in frontotemporal sub-regions for the dual reading routes (Jobard et al., 2003). In adults, the grapho-phonological processing relies on opercularis part of left IFG and left STG, while the lexico-semantic processing relies on orbitalis part of left IFG and left MTG (Poldrack et al. 1999; Devlin et al. 2003; McDermott et al. 2003; Price and Mechelli 2005; Friederici 2011; Price 2012; Binder 2016). There is only one recent study that directly compared the early specialization of brain regions for phonological and semantic processing of spoken language during early childhood (5-6 years) using an auditory rhyme and semantic judgment tasks, respectively (Weiss et al. 2018). They reported overlap in activity in the bilateral frontotemporal cortex for the two tasks. On comparing the activity differences between the two tasks using subtraction based univariate analysis, they found specialization of left STG and left SMG for phonological processing, and left MTG for lexical processing. Their results suggested that the temporal cortex is already specialized for spoken language by five years of age. However, they did not observe any task differences in the left IFG sub regions and suggested that frontal areas may not be specialized for spoken language processing in children by the age of five. Our MVPA results suggested specialization of the left IFG opercularis for phonological processing. The MVPA results also indicated no specialization in IFG sub-regions for semantic processing. The cluster peak in IFG orbitalis that successfully decoded semantic task condition, extends to IFG opercularis and IFG triangularis. Thus, our findings suggest that IFG sub-regions are specialized in early childhood for phonological processing but not for semantic categorization. We did not find specialization of temporal sub-regions as observed by Weiss et al. (2018), which might be attributed to the modality of stimuli, visual-only stimuli (this study) versus audio-only stimuli (Weiss et al. 2018).

4.2.2 Parietal lobe

Our univariate and multivariate results indicate that bilateral parietal areas (supramarginal, precuneus and angular gyrus) are recruited for semantic categorization, but not for phonological decision-making. In adults, using univariate methods, the regions of the semantic network, including bilateral angular gyrus, anterior temporal lobe, ventromedial prefrontal cortex and precuneus have been shown to activated for meaningless nonwords (Binder et al. 2005; Wang et

al. 2010). Moreover, using multivariate methods, the same regions have been shown to represent information for decoding words along the semantic dimension, high versus low imageability (Mattheiss et al. 2018). For children of age nine years and above, the left IPL and angular gyrus have been reported to be specialized for semantic categorization tasks (Booth et al., 2007, Landi et al., 2010). Our study provides evidence of bilateral parietal involvement for semantic decision making even in young children (5-7 years of age). On the contrary, Weiss et al. (2018) did not find parietal specialization for semantic categorization task using auditory stimuli for young children (5-6 years of age) and instead they argued that parietal areas might specialize for semantic processing only later in development. We predict that perhaps visual stimuli implemented in this study require high imageability for semantic decision making and thus bilateral parietal areas are recruited for visual semantic categorization task in young children.

4.2.3 Fusiform Gyrus

The role of a portion of the fusiform gyrus, the letterbox region called the VWFA, has been suggested for decoding letter strings to words (McCandliss et al. 2003). A decrease in activation in the right VWFA at a location in the right hemisphere that is precisely symmetrical with the letterbox region has been reported with increase in age (Turkeltaub et al., 2003). It has been reported that written words, like any other visual image, lead to bilateral activation pattern. Activation then progressively tapers down to a narrower focus that is presumably optimal in left hemisphere (Dehaene 2009). This finding is consistent with past research on older children that report VWFA is already visible in its adult location in the left occipito-temporal cortex by the age of seven (Gaillard et al. 2003; Parviainen et al. 2006). Our MVPA results indicate that VWFA is already specialized to left hemisphere by early childhood (5-7 years of age).

While some authors postulated that the VWFA is dedicated to the lexico-semantic route only (Levy et al. 2009), others assume that VWFA is common for both grapho-phonological and lexico-semantic routes and information is then be passed on to the most appropriate route to read a word (Jobard et al. 2003; Goswami 2008). Our findings suggest that the left VWFA is recruited for both pre-reading routes during early childhood.

Conclusion

In conclusion, this is the first study to use multivariate methods to understand the specialization of grapho-phonological and lexico-semantic reading routes in early childhood (5-7 years of age). Specifically, by using MVPA methods, we observed left hemisphere specialization for grapho-phonological route. We provide evidence that children with good reading ability have already established the grapho-phonological reading route in the brain, that includes the left fusiform gyrus, STG/MTG, and IFG, to support the early stages of reading. Moreover, lexico-semantic processing also relies on left hemisphere areas, including the left fusiform gyrus, STG/MTG, and IFG, as well as require additional recruitment of the bilateral parietal areas. The involvement of the bilateral parietal areas has been related to retrieval of semantic information in adults (Binder and Desai 2011). Our results in young children indicate neural specialization of semantic information retrieval has already been established by five years of age. Our MVPA results also indicate IFG opercularis specialization for the phonological reading route in early childhood, as observed in previous research for adults (Jobard et al. 2003), and school-age children (Bach et al. 2010). However, our study does not show evidence for temporal specialization for the phonological processing and fronto-temporal specialization for the semantic processing. On the contrary, using an auditory rhyme and semantic judgment tasks, Weiss et al. (2018) reported the specialization for the phonological processing in the left STG and SMG, and the specialization for the semantic processing in the left MTG by the age of 5-6-years. Some differences between our findings and results from Weiss et al. (2018) could be attributed to modality of stimuli. Future within-subject design studies will be helpful to determine the effect of modality (visual versus auditory) in neural specialization of phonological and semantic processes in early childhood.

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Author Contribution Statement

Mathur, A. conceived and planned the experiments, analyzed the data, drafted the manuscript and designed the figures with support from Wang, Y. Schultz, D. discussed data analysis methodology with Mathur, A. Wang, Y. supervised the project.

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Disclosure Statement

The authors declare that no competing financial interests exist.

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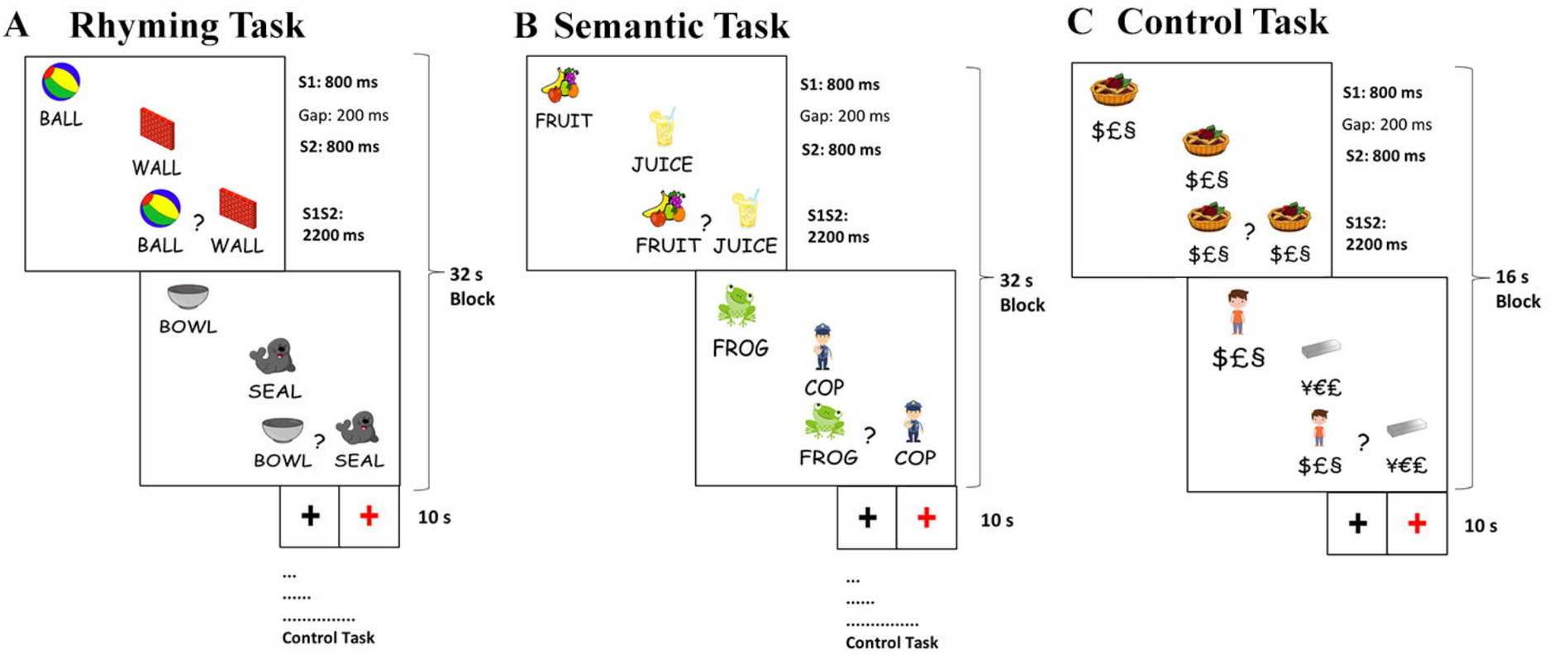

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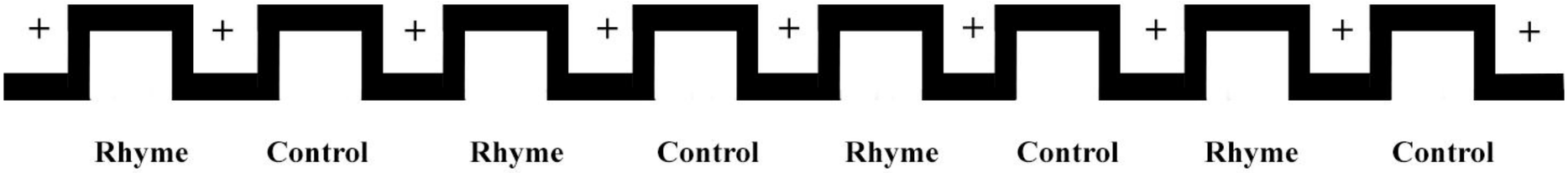
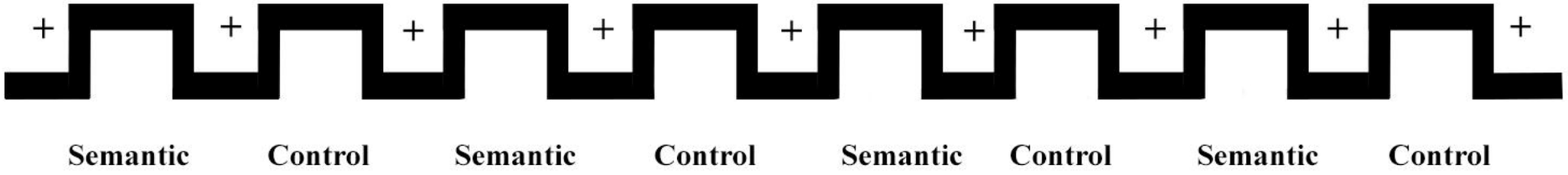
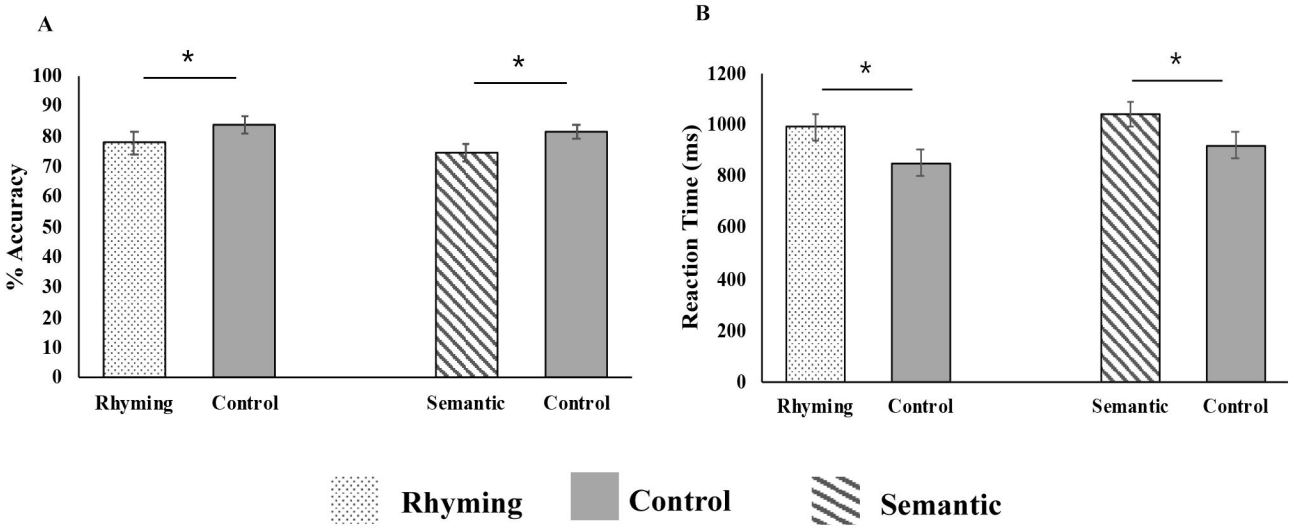
Rhyming Run



Semantic Run

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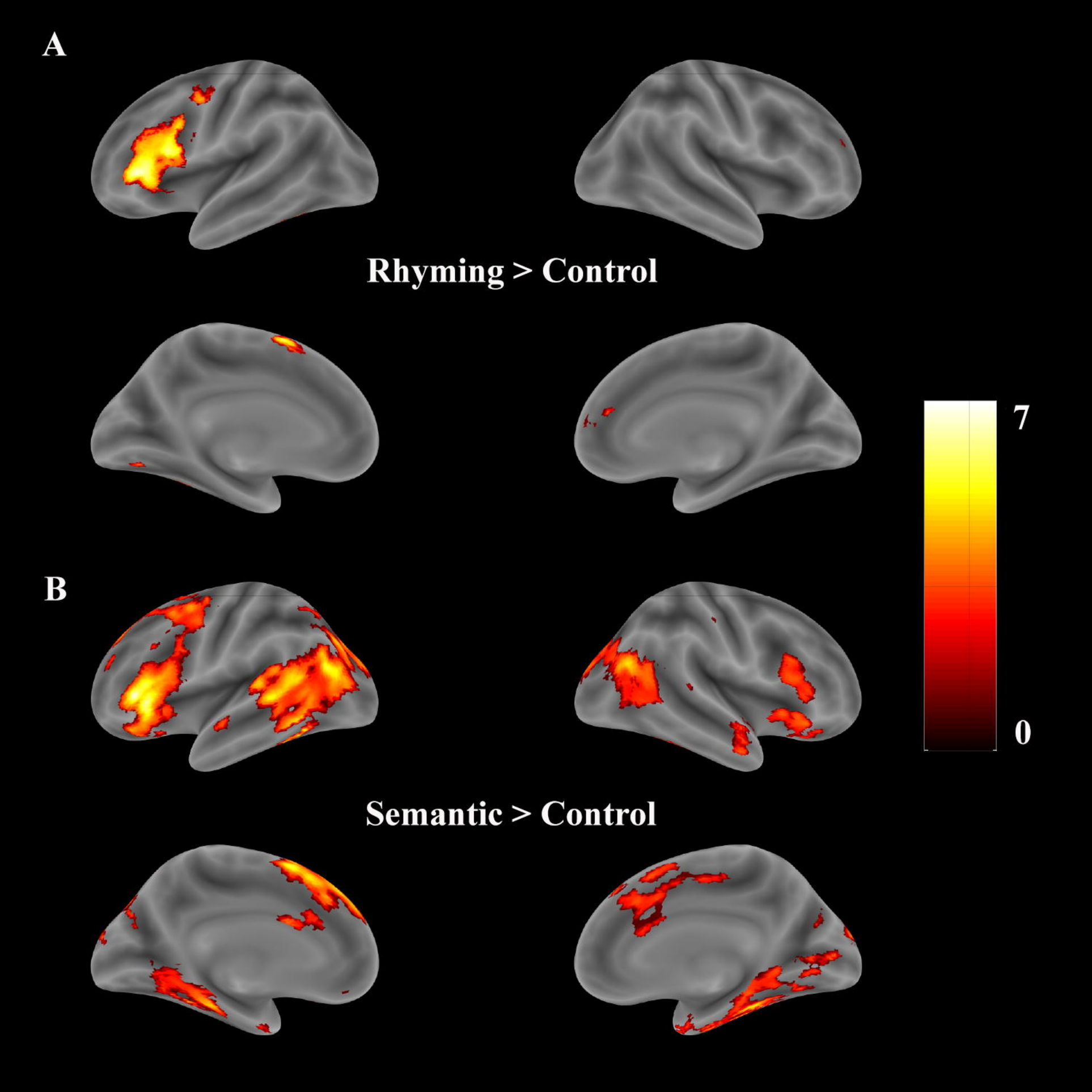
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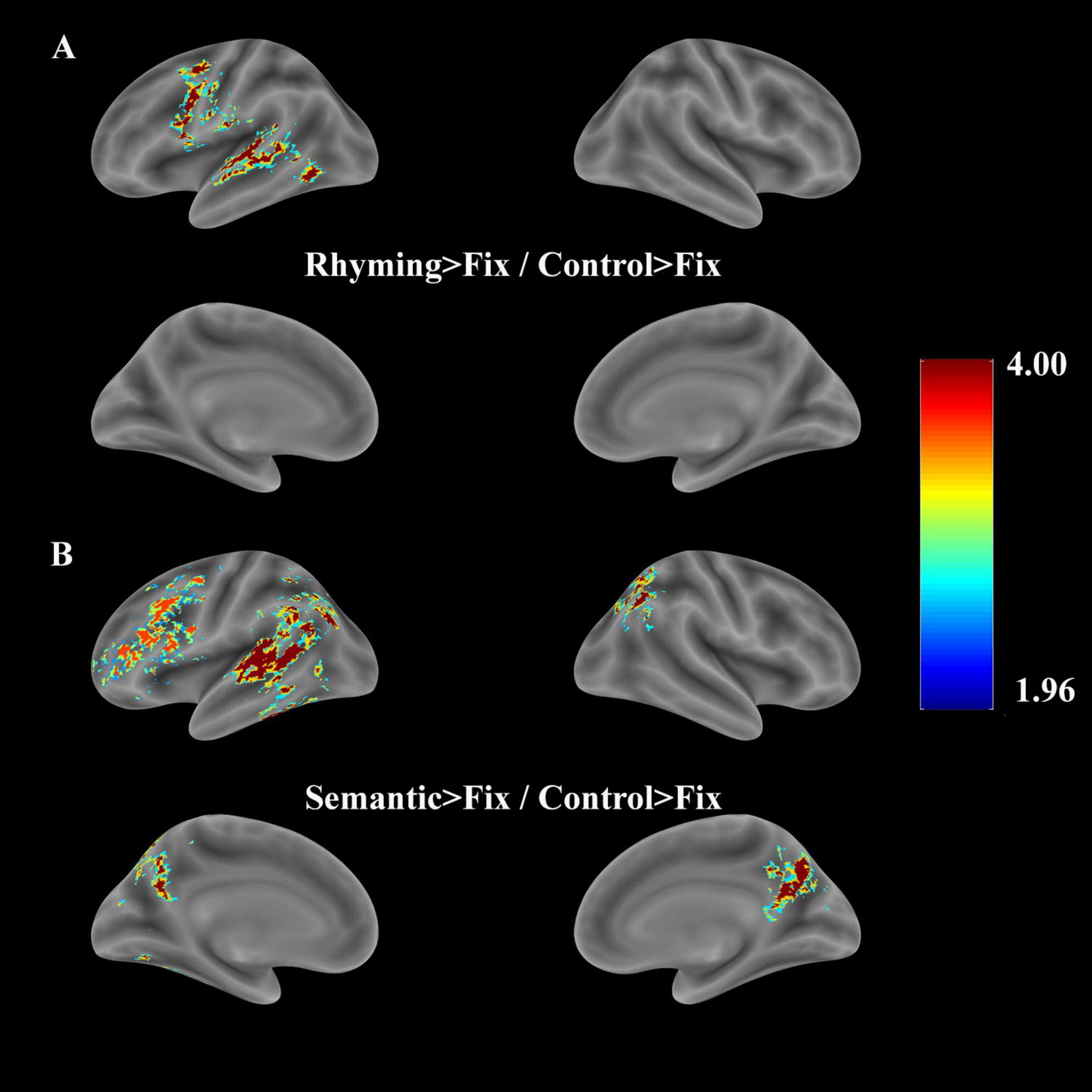
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Figure Legends

Figure 1. Schematic representation of fMRI task design.

Figure 2. Average (N=19) in-scanner task accuracy and reaction time.

Figure 3. Voxel-wise significant activation, within the whole brain anatomical mask for the contrast (A) rhyming vs control and (B) semantic vs control. The significant clusters were identified using a voxel-wise threshold of $q < 0.05$, FDR correction at a cluster threshold $k > 20$.

Figure 4. Multivariate Pattern analysis results. Statistical group maps for the two-searchlight analysis performed with a 100-voxel searchlight using LDA classifier to identify regions that significantly decode above chance (A) rhyme from control condition and (B) semantic from control condition. The resulting statistical maps were corrected for multiple comparisons using a cluster-based Monte Carlo simulation algorithm implemented in the COSMOMVPA toolbox [Oosterhof et al., 2016, clusterstat maxsum function] (corrected cluster threshold $\alpha = .01$, two-tailed; $z > 1.96$).

Supplementary Figure 1. Rhyming vs Control contrast at 0.01 uncorrected, $k > 20$.

Table 1. In-scanner Performance

	Rhyme Task		Paired T-tests	Semantic Task		Paired T-tests
	Rhyme	Control		Semantic	Control	
Accuracy (%)	77.1 ± 16.2	83.4 ± 11.8	$p < 0.05$	74.7 ± 13.0	82.6 ± 9.5	$p < 0.05$
Reaction time (ms)	1004.8 ± 222.4	874.93 ± 196.0	$p < 0.05$	1060.2 ± 194.6	946.2 ± 185.7	$p < 0.05$

Table 2. Univariate results for the contrast Rhyme vs Control. The table includes all the peaks of the significant clusters within the functional mask.

Region	L/R	BA	MNI Coordinates			Cluster Size	z-value
			x	y	z		
Frontal							
IFG (p. tri, op., orb.)	L	44/45/47	-50	34	3	1554	5.55
IFG (p. tri)[1]	R	45	52	34	3	187	3.23
SMA	L	6	-2	6	63	190	5.38
DLPFC[1]	L	9	0	52	36	65	2.81
DLPFC	R	9	15	52	13	72	3.71
Parietal							
Precentral Gyrus	L	4	-48	-4	50	104	4.46
Pre/Postcentral[1]	R	3	50	-1	50	35	2.90
Temporal							
ITG (Fusiform)	L	37	-42	-34	-17	111	3.63
STG/MTG[1]	L	22/21	-55	-36	6	116	3.57
STG/MTG[1]	R	22/21	48	-36	6	41	2.78

Note. Activity peaks reported at a significant voxel threshold of $q < 0.05$, FDR corrected, cluster size, $k > 20$.
Note[1]. The activity is reported at uncorrected threshold of $p < 0.01$, cluster size, $k > 20$, refer to supplementary Figure 1.
(IFG - Inferior Frontal Gyrus (p. triangularis, p. opercularis and p. orbitalis), SMA - Supplementary Motor Area, PFC - Prefrontal Cortex, ITG- Inferior Temporal Gyrus, MTG - Middle Temporal Gyrus, STG - Superior Temporal Gyrus.)

Table 3. Univariate results for the contrast Semantic vs Control. The table includes all the peaks of the significant clusters within the functional mask.

Region	L/R	BA	MNI Coordinates			Cluster Size	z-value
			x	y	z		
Frontal							
IFG *	L	44/45/47	-45	32	3	5177	5.59
Parietal							
Pre/Post-central Gyrus	R	3/4	55	-11	53	83	3.17
IPL (Supramarginal, precuneus and angular Gyrus)	L/R	40/39					
Temporal							
MTG/ITG (Fusiform Gyrus)	L	21/37	-45	-51	-12	7324	5.00
MTG/ITG (Fusiform Gyrus)	R	21/37	68	-41	6	42	2.91

Note. Activity peaks reported at a significant voxel threshold of $p < 0.05$, FDR corrected, cluster size, $k > 20$.
Note*. The cluster activation extends from the peak activity in left IFG (p. triangularis, p. opercularis and p. orbitalis), to left MFG, left precentral gyrus, left SMA and right IFG (p. triangularis and p. orbitalis).
(IFG - Inferior Frontal Gyrus, ITG - Inferior Temporal Gyrus, MTG - Middle Temporal Gyrus, IPL - Inferior Parietal Lobe, SMA - Supplementary Motor Area)

Table 4. MVPA searchlight results for Rhyme vs Control.

Region	L/R	BA	MNI Coordinates x	y	z	Extent	z-value
Frontal							
Pre/Postcentral Gyrus	L	6	-60	-14	31	1380	2.878
IFG (p. op.)	L	44	-35	7	31		
Temporal							
MTG/STG	L	21/22	-55	-14	-10	1380	2.878
ITG (Fusiform Gyrus)	L	37	-48	-66	-15		

Note. The table above lists the brain areas that successfully classify rhyme from control condition at a cluster corrected threshold, $p < 0.01$
(IFG – Inferior Frontal Gyrus, MTG – Middle Temporal Gyrus, STG – Superior Temporal Gyrus, ITG – Inferior Temporal Gyrus)

Table 5. MVPA searchlight results for Semantic vs Control.

Region	L/R	BA	MNI Coordinates x	y	z	Extent	z-value
Frontal							
IFG (p. orbitalis) *	L	45	-35	29	-15	1680	2.327
Temporal							
MTG/STG	L	21/22	-53	-11	3	3762	2.878
ITG (Fusiform gyrus)	L	37	-45	-61	-5		
Parietal							
IPL (Supramarginal, precuneus and angular Gyrus)	L	39/40					
IPL (Supramarginal, precuneus and angular Gyrus)	R	39/40					

Note. The table above lists the brain areas that successfully classify semantic from control condition at a cluster corrected threshold, $p < 0.01$.
Note*. Left IFG (p. orbitalis) cluster extends to left IFG (p. triangularis, p. opercularis), left precentral gyrus (BA 6) and MFG (BA 46)
(IFG – Inferior Frontal Gyrus, MTG – Middle Temporal Gyrus, STG – Superior Temporal Gyrus, ITG – Inferior Temporal Gyrus, IPL – Inferior Parietal Lobe)