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Functional connectivity in resting state as a phonemic fluency ability measure

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ABSTRACT

There is some evidence that functional connectivity (FC) measures obtained at rest may reflect individual differences in cognitive capabilities. We tested this possibility by using the FAS test as a measure of phonemic fluency. Seed regions of the main brain areas involved in this task were extracted from meta-analysis results (Wagner et al., 2014) and used for pairwise resting-state FC analysis. Ninety-three undergraduates completed the FAS test outside the scanner. A correlation analysis was conducted between the F-A-S scores (behavioral testing) and the pairwise FC pattern of verbal fluency regions of interest. Results showed that the higher FC between the thalamus and the cerebellum, and the lower FCs between the left inferior frontal gyrus and the right insula and between the supplementary motor area and the right insula were associated with better performance on the FAS test. Regression analyses revealed that the first two FCs contributed independently to this better phonemic fluency, reflecting a more general attentional factor (FC between thalamus and cerebellum) and a more specific fluency factor (FC between the left inferior frontal gyrus and the right insula). The results support the Spontaneous Trait Reactivation hypothesis, which explains how resting-state derived measures may reflect individual differences in cognitive abilities.

KEYWORDS

Resting-state; Functional Connectivity; Verbal Fluency; fMRI; Individual Differences

1. Introduction

In neuroimaging research, for years the existence of brain activity without performing any cognitive task (i.e., intrinsic or spontaneous brain activity) was considered a very low frequency random noise and, therefore, excluded. Recent studies have shown that this activity is not random, but rather well-structured and organized (Biswal, Yetkin, Haughton, & Hyde, 1995; De Luca, Smith, De Stefano, Federico, & Matthews, 2005). This "resting-state" activity has a similar amplitude to what appears during task performance, and it covers the entire brain cortex (Nir, Hasson, Levy, Yeshurun, & Malach, 2006). A further step in research on this spontaneous activity is to give a "cognitive value" to this information.

Some studies have found significant correlations between individual differences in spontaneous connectivity patterns and differences in individual task performance. Harmelech and Malach (2013) tried to unify the quantity of resting-state data under a single principle. They proposed the "spontaneous trait reactivation" hypothesis (STR), which basically states that spontaneous fluctuations could teach us about individual personality traits, abilities, and even diseases. They tested their hypothesis by reviewing a number of studies using different measures. One of these measures was individual differences in cognition. Our study aims to contribute more empirical evidence to the STR hypothesis by using a resting-state FC data analysis approach to investigate the possible individual differences when performing a verbal phonemic fluency task.

Previous results of resting-state studies agree with this proposal of using functional connectivity (FC) measures. Resting-state FC provides information about the profile of each person's neuronal connectivity biases and focuses on connectivity assessed across individual BOLD time points during resting conditions (Friston, 2009). For example, Ventura-Campos et al. (2013) showed a method for studying the brain's capacity to learn by determining FC during resting-state-fMRI (rs-fMRI) between task-related brain areas. The authors concluded that spontaneous brain activity predicts the ability to learn foreign sounds. Their work used the methodology from a study by Baldassarre et al. (2012), where a correlation between individual differences in performance on a perceptual task and dissimilarities in resting-state functional connectivity (rs-FC) were demonstrated. Another study showed the predictive properties of resting state fluctuations in individual performance after learning (Lewis, Baldassarre, Committeri, Romani, & Corbetta, 2009). In addition, measures of the intrinsic brain activity synchronization within a region (i.e., regional homogeneity) during resting-state have predicted individual differences on a variety of cognitive tasks (Barttfeld et al., 2013; Coste, Sadaghiani, Friston, & Kleinschmidt, 2011; Martin, Barnes, & Stevens, 2012; Mennes et al., 2010; Wang et al., 2013; Zou et al., 2013).

Verbal fluency is an executive function that neuropsychological language production tests easily evaluate. These tests evaluate the capacity to generate words in a fixed time, usually one minute. Generally, participants have to say as many words as possible from a specific category. Categories can be semantic (produce names such as animals or fruits) or phonemic (generate words beginning with a specific letter). Those kinds of tasks require subjects to retrieve words stored in the long-term memory, and they involve frontal processes. Successful retrieval requires executive control over cognitive processes such as selective attention, working memory, language production, mental set shifting, internal response generation, and inhibition of inappropriate responses (Lezak, 1995; Patterson, 2011; Ruff, Light, Parker, & Levin, 1997).

Several investigations have studied the neural basis of verbal fluency (Gauthier, Duyme, Zanca, & Capron, 2009; Heim, Eickhoff, & Amunts, 2008; Weiss et al., 2004; Weiss, 2003). In a meta-analysis, Wagner et al., (2014) included twenty-eight individual studies with a total of 499 healthy volunteers to separately study the brain areas involved during the performance of phonemic and semantic verbal fluency tasks. The authors found eight regions with significant activation during phonemic verbal fluency tasks, and seven regions with significant activation during semantic verbal fluency tasks. In the case of phonemic fluency, the area most involved was the left inferior frontal gyrus (LIFG), a brain area implicated in word production and speech processing on different tasks, especially phonemic fluency (Broca, 1861; Bookheimer, 2002; Demonet, Fiez, Paulesu, Petersen, & Zatorre, 1996; Hirshorn & Thompson-Schill, 2006; Indefrey & Levelt, n.d.; Price, 2000, 2010). Neuropsychological studies have revealed that patients with lesions in the left frontal lobe were more impaired in phonemic fluency than those with right frontal lesions (Robinson, Shallice, Bozzali, & Cipolotti, 2012). Although right inferior frontal activation has been related with semantic tasks (sentence comprehension) (Price, 2010), it is also relevant because has been associated with attentional switching and response inhibition (Hampshire, Chamberlain, Monti, Duncan, & Owen, 2010). The left insula was also strongly involved in phonemic processing and during the performance of the verbal fluency task (Brown et al., 2009; Gauthier et al., 2009; Price, 2010; Saur et al., 2008). Some studies have also related the insula to vocal production (Ackermann & Riecker, 2004; Riecker, Ackermann, Wildgruber, Dogil, & Grodd, 2000). Other brain structures associated with phonemic fluency were the thalamus, the cerebellum and the supplementary motor area (SMA). On the one hand, activations of the thalamus have been associated with processing stages during verbal fluency tasks (Llano, 2013) and activations in the cerebellum have been related to speech production (Price, 2010), selecting correct responses and attention (Senhorini et al., 2011). On the other, the SMA has been related to the cognitive effort linked to word selection processes, in addition to its role during the encoding of word form information and overt language articulation (Alario, Chainay, Lehericy, & Cohen, 2006; Price, 2010).

The present study was designed to verify whether resting-state activity serves as a good verbal fluency ability measure. We will compare the resting-state FC of brain areas with significant activation on a phonemic fluency task to the performance on a phonemic fluency task. In agreement with the STR hypothesis and bearing in mind the results of previous investigations where resting-state FC has been able to describe individual differences in the performance on cognitive tasks, our main hypothesis was that FC patterns would be able to describe individual differences on the phonemic fluency task at the brain level. We hypothesized that participants with more coherent FC patterns will perform better on the phonemic fluency task.

2. **Materials and methods**

2.1. Participants

Ninety-three right-handed, healthy undergraduates (37 male) with ages ranging between 18-30 years (mean age = 20.65; SD = 2.697) participated in this study. They were native Spanish speakers, and none of them had a previous psychiatric or neurologic diagnosis. Informed consent was obtained from each subject before participation, and they received monetary compensation for their time and effort. The Ethical Committee of Universitat Jaume I approved the research project.

2.2. Behavioral task

The Spanish version of the FAS test (Spreen & Benton, 1977) was completed by all participants a day before the resting-state fMRI session. During the phonemic fluency tasks, participants were asked to orally produce as many words as possible beginning with a requested letter (F, A or S) within a prescribed time frame (a minute).

2.3. Neuroimaging data acquisition

Functional MRI sessions consisted of a resting-state scan where participants were instructed to simply rest with their eyes closed and try not to sleep or think about anything in particular. Images were acquired on a 1.5 T scanner (Siemens Avanto). Participants were placed in a supine position in the MRI scanner, and their heads were immobilized with cushions to reduce motion artifacts. For the rs-fMRI, a total of 270 volumes were recorded over 9 min, using a gradient-echo T2*- weighted echo-planar imaging sequence (TR = 2000 ms; TE = 48 ms; matrix, 64 x 64; voxel size = 3.5 x 3.5 mm; flip angle = 90°; slice thickness = 4 mm; slice gap = 0.8 mm). We acquired 24 interleaved axial slices parallel to the anterior–posterior commissure plane covering the entire brain. Before the functional magnetic resonance sequences, a high-resolution structural T1-weighted MPRAGE sequence was acquired (TR = 2200 ms; TE = 3.8 ms; matrix = 256 x 256 x 160; voxel size = 1 x 1 x 1 mm).

2.4. Behavioral data analyses

Descriptive analyses were conducted with SPSS (v.21, Armonk, New York, USA). The mean F-A-S score was calculated for each participant and subsequently used in resting-state FC correlation analyses. In addition, the data sample distribution was studied, along with the mean and the standard deviation.

2.5. Resting-state Functional Connectivity analyses

2.5.1. Preprocessing

Rs-fMRI datasets were processed using a toolkit of the Data Processing Assistant for Resting-State fMRI (DPARSFA; http://rfmri.org/DPARSF) (Yang & Zang, 2010), based on some Statistical Parametric Mapping functions (SPM v.8 Wellcome Trust Centre for Neuroimaging, London, UK) to preprocess the rs-fMRI data and REST software (http://www.restfmri.net) for the connectivity analysis. Prior to preprocessing, we applied artifact correction (automatic detection and reparation of bad slices) with the ArtRepair toolbox for SPM (Mazaika, Whitfield-Gabrieli, & Reiss, 2007). The rs-fMRI preprocessing included the slice-timing correction for interleaved acquisitions using sinc-interpolation and resampling with the middle slice (24^{th}) in time as the reference point. Head motion correction was performed, where the functional images were realigned and resliced to the mean functional image. Afterwards, the anatomical image (T1-weighted) was co-registered to the mean functional image, and the transformed anatomical image was then segmented by the new segment + DARTEL. We conducted additional preprocessing through the following steps: (i) removing the linear trend + quadratic trend in the time series and (ii) controlling the non-neural noise in the seed region time series (Fox et al., 2005). Several sources of spurious variance were removed from the data through linear regression: six parameters from rigid body correction of head motion, the global mean signal, the white matter signal, and the cerebrospinal fluid signal. Recently, head motion has been shown to differentially impact FC measures, which can introduce spurious correlations in the FC analyses (Power, Barnes, Snyder, Schlaggar, & Petersen, 2012; Satterthwaite et al., 2012; Van Dijk, Sabuncu, & Buckner, 2012). To assess this potential confounding effect, we performed the scrubbing of each participant using the *F*D Jenkinson procedure with a threshold for "bad" time points of 0.2 (one time point before and two "bad" time points after). The scrubbing method was to use each bad point as a regressor. The functional images were spatially normalized to the MNI (Montreal Neurological Institute, Montreal, Canada) space with a 3 mm^3 resolution using the normalization by DARTEL and spatially smoothed with an isotropic Gaussian kernel of 4 mm FWHM (Full-Width at Half-Maximum). Finally, we used temporal band-pass filtering (0.01-0.08 Hz) to reduce the effect of low-frequency drift and high-frequency noise (Biswal et al., 1995; Lowe, Mock, & Sorenson, 1998).

2.5.2. *Seed-voxel selection*

As our main objective was to study resting-state FC patterns of brain areas involved in the performance of phonemic fluency tasks and the information that these FC patterns provide about individual differences in verbal fluency, specific regions of interest were used in our rs-fMRI analyses. Therefore, the seed regions selected for the rs-fMRI analysis were extracted from the Wagner et al. (2014) meta-analysis of neuroimaging studies using the phonemic fluency task. A total of six ROIs were made (see Table 1), and they were built with the WFU Pickatlas toolbox (Maldjian, Laurienti, Kraft, & Burdette, 2003), obtaining spheres with a 6 mm radius used in the FC analyses. We selected the six most relevant ROIs from that study in terms of the number of studies reporting at least one activation peak.

Table 1. Regions with significant activation during phonologic verbal fluency (Wagner et al., 2014) included in our resting-state pairwise FC analysis as seed regions.

Region	Brodmann Area	MNI coordinates
Left Inferior Frontal Gyrus (LIFG)	44	-50 12 24
Left Insula (LIns)	13	-44 18 6
Supplementary Motor Area (SMA)	32	-2 14 48
Right Insula (RIns)	13	44 16 -12
Thalamus		-2 -18 6
Right Cerebellum		36 -60 -32

2.5.3. *Seed-based rs-FC analyses*

After the preprocessing of the rs-fMRI data, we used the predefined seed regions for ROI-wise rs-FC analyses using the DPARSFA toolbox. The mean time course of all the voxels in each seed region was used to calculate pairwise linear correlations (Pearson's correlation) during each rs-fMRI period. Individuals' r values were normalized to z values using Fisher's *z* transformation. Then, FC ROI-wise analyses (pair correlations between ROIs) were conducted. Pearson's correlations and multiple regression analyses were performed using the SPPS (v.21, Armonk, New York, USA) in order to study the relationship between phonemic fluency task scores and brain activity during the rest condition. We analyzed the association between phonemic fluency task performance and FC in the selected areas by correlating the mean F-A-S score for each subject and the mean activity value in the specific brain areas of interest. Bonferroni-Holm corrections for multiple comparisons adjusted for dependent measurements were performed for all correlations (k = 15). In addition, we used the opposite-hemispheric homolog from our six regions of interest (Palomar-García, Zatorre, Ventura-Campos, Bueichekú, & Ávila, 2016) in order to make sure that the F-A-S score is not correlated with the FC of areas that are not involved during phonemic fluency tasks. In fact, we added three more ROIs (rIFG, right Thlamaus and left cerebellum). We cannot included homologs for the Insula (because both were involved) and the SMA (because the homolog was included in the ROI). Our regression analysis was restricted to the regions of interest described above in areas with significant activation during phonemic fluency tasks. A multiple regression using the stepwise method was conducted to determine whether the seed regions predict good phonemic fluency performance using the mean FAS scores as the dependent variable and the FC that significantly correlated with FAS scores as independent variables.

3. Results

3.1. Behavioral data

The results of the phonemic fluency task (FAS Test) showed the following findings: the mean of the number of words was 35.76 (SD = 8.33; range = 38). Our data follow a normal distribution ($D_{93} = .063$ $p > 0.05$), with a maximum score of 56 and a minimum score of 18.

3.2. rs-FC results

To determine whether the rs-FC is a good predictor of phonemic fluency performance, we calculated the correlations between mean F-A-S scores and brain activity in seed regions during the rest condition. All the values were positive but moderate. On the one hand, Pearson's correlations yielded significant negative correlations between phonemic fluency scores and the FC of the Left Inferior Frontal Gyrus-Right Insula and Left SMA-Right Insula pairs. However, the Left SMA-Right Insula was not significant if corrected for multiple comparisons. On the other hand, a significant positive correlation was found between F-A-S scores and the FC between the thalamus and the cerebellum. See Table 2 for mean scores, standard deviations, and correlation analysis results, and Figure 1 for scatterplots of the meaningful correlations. We found no significant results in the opposite-hemispheric homolog correlation.

To identify the FCs that will influence the phonemic fluency ability, a multiple regression analysis was conducted using the stepwise method. Stepwise regression fundamentally performs a multiple regression a number of times, each time adding the weakest correlated variable, and resulting in the variables that best explain the distribution. Stepwise adds a variable that contributes to the model. We used mean F-A-S scores as the dependent variable and the three FC values that significantly correlated with the F-A-S scores (pairs Left Inferior Frontal Gyrus-Right Insula, Left SMA-Right Insula and Thalamus-Cerebellum pairs) as independent variables. The regression model (corrected $R^2 = .144$; $F_{2,9} = 8.75$, $p < 0.001$) was reached in two steps and contained two of the three predictor pairs, the Left Thalamus-Right Cerebellum and the Left Inferior Frontal Gyrus-Right Insula (see Table 3). In the first step, the FC between the Left

Thalamus and Right Cerebellum were entered in the model and explained the 7.8% of the variance. In the second step, the FC between the Left Inferior Frontal Gyrus and the Right Insula were entered in the model and and explained an additional 6.6% of the variance.

Table 2. Resting state FC analysis results. Above the diagonal: Means and standard deviations of FC measures between ROIs. Below the diagonal: correlations (r) between F-A-S Test scores and FC measures between ROIS. LIFG: left inferior frontal gyrus. LIns: left insula. LSMA: left supplementary motor area. RIns: right insula.

	LIFG	**LIns**	**LSMA**	**RIns**	**LThalamus**	**RCerebellum**
LIFG	-	M=.124 SD=.167	M=.178 SD=.193	M=.022 SD=.138	M=-.054 SD=.159	M=.028 SD=.145
LIns	.04	-	M=.214 SD=.192	M=.153 SD=.171	M=.074 SD=.153	M=.074 SD=.148
LSMA	-.13	.00	-	M=.132 SD=.194	M=.088 SD=.165	M=.187 SD=.166
RIns	-.30**	-.14	-.21*	-	M=.128 SD=.167	M=-.003 SD=.158
LThalamus	.03	.16	-.12	.03	-	M=.159 SD=.158
RCerebellum	-.08	.16	-.00	.01	.30**	-

* P < .05, uncorrected; ** p < .05, corrected for multiple comparisons

Figure 1. Significant correlations between F-A-S scores and **(A)** Left Inferior Frontal Gyrus-Right Insula, (B) Left SMA-Right Insula and, (C) Thalamus-Cerebellum.

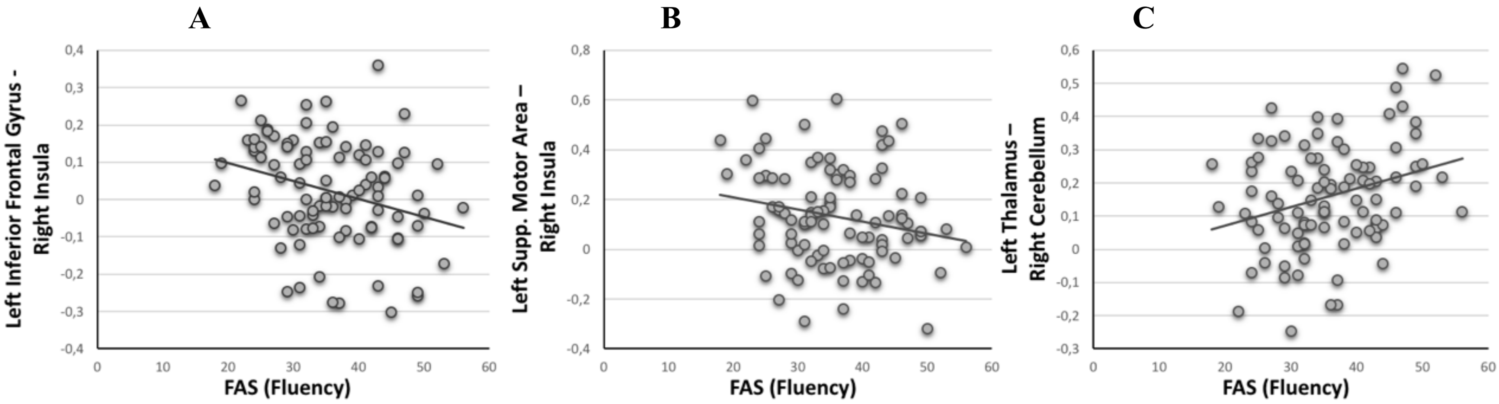

Table 3. Main predictors of phonemic fluency task performance as a result of the multiple regression stepwise analysis. LIFG: left inferior frontal gyrus. RIns: right insula.

Predictor Variable	Beta	*P*
Left Thalamus - Right Cerebellum	.280	0.005
LIFG – RIns	-.274	0.006

4. Discussion

In the current study, we investigated the capacity of FC at rest between target areas involved in the phonemic fluency task in order to predict the performance on the same task performed outside the scanner. We administered the FAS version of the fluency task, and then we registered the BOLD activity in the entire brain during rest. We identified the main areas involved in the task, including the lateral prefrontal cortex, insula, and subcortical structures from the local maxima obtained in a recent meta-analysis on the task, and we calculated the FC between them. Results showed that the FC between some of these areas correlated positively or negatively with performance on the FAS. Importantly, regression analysis showed that the multiple correlation of two of the FCs explained 14.4% of the variance in FAS performance, demonstrating that different variables account for different sources of variance. Although all the correlations were of moderate strength, resting-state fMRI may be a good technique for estimating cognitive capabilities of individuals.

The current study presents a new methodology for on determining the main brain areas involved in the task based on data from a relevant study (i.e. in our case, from a meta-analysis summarizing data from 23 experiments and 499 participants) and calculating the FC between them. The methodology makes it possible to contribute empirical evidence to the STR hypothesis that resting-state BOLD activity may reflect a priori cognitive biases in the brain. We then expected to predict performance on the task based on the connectivity between these main foci. Although the magnitude was moderate, the results confirmed that some FC measures between main distant brain areas were significantly positively or negatively correlated with performance on the task. According to the STR hypothesis, each of these FCs may represent the capability of these areas to perform a cognitive process involved in the task. Notably, the multiple correlations of some of these measures with performance indicate that these FCs explained different sources of variance in cognitive capability, indicating that they may be representing different cognitive processes involved in the task.

Verbal Fluency is a test commonly used for neuropsychological assessment in both clinical and research settings that assess executive function and the spontaneous production of words under restricted search conditions (Lezak, Howieson, Bigler, &

Tranel, 2012). Phonemic fluency is considered a reflection of executive function because it requires a capacity for verbal retrieval and recall, self-monitoring, effortful self-initiation, and response inhibition (Henry & Crawford, 2004). The different cognitive processes may be associated with the connectivity among the different areas involved in the task. In this sense, five main brain areas have been involved in this task: the anterior insula/ inferior frontal gyrus, the SMA and, finally, subcortical structures such as the thalamus and the cerebellum.

As expected, one of the most important areas where FC is relevant in predicting performance is the anterior insula/inferior frontal gyrus (Costafreda et al., 2006). This area has been involved in executive control and response selection of target words, the dynamic allocation of attentional resources, and filtering out unwanted stimuli during fluency tasks. Although the left part is more involved in the task, the right inferior frontal cortex/insula is also relevant because of the need to inhibit inappropriate responses (Costafreda et al., 2011). Overall, these executive control components contribute to maintaining task performance during verbal fluency. Our results showed that stronger negative FC between the left inferior frontal gyrus and the right insula was associated with better performance on phonemic fluency.

The second area is the SMA. It is involved in task monitoring, conflict detection, and response suppression during executive tasks, and it has a more prominent role when the task is difficult (Price, 2012). The SMA appears to be involved in phonologic fluency, but not in semantic fluency (Wagner et al., 2014). According to the authors, phonemic fluency involves processes of inward speech, such as motor programming and articulation, as indicated by activations of the SMA. Although the correlation did not reach significance when corrected for multiple comparisons, our results showed a negative trend indicating that less FC between this area and the right insula was associated with better performance on the FAS task. SMA lesions in humans are associated with transcortical motor aphasia and transient mutism. Thus, the SMA appears to be involved in the initiation and maintenance of speech. This role contrasts with the aforementioned inhibitory influences reported for the right insula. Thus, it is reasonable to speculate that less FC between the two areas would facilitate fluency on fluency tasks.

Finally, two subcortical structures were involved. The positive FC between the thalamus and the cerebellum was associated with better performance on the fluency task. The thalamus has been involved in language tasks that require the manipulation of lexical information, especially when tasks have a high attentional demand (Llano, 2013). The cerebellum has a more controversial role. Lesions in the right cerebellum typically impair performance on fluency tasks. Initially, this poor performance was attributed to slowness in language processing (Holmes, 1917), but it has been obtained even when controlling for response speed (Stoodley & Schamahmann, 2009). In the same vein, a recent study showed that the same region of the right cerebellum was more associated with phonemic fluency performance during the easier version of the task than during the difficult one (Senhorini et al., 2011). The authors attributed to this area a role in selecting correct responses and paying attention to performance. Thus, the FC between the thalamus and the cerebellum may be associated with the requirement of attending to and monitoring correct responses.

Regression analysis with all of the significant FCs revealed that two of these associations accounted for different sources of variance. The first is the FC between the left inferior frontal gyrus and right insula, reflecting the language component of fluency (i.e. selecting words, inhibiting competitors), whereas the second was the FC between the cerebellum and the thalamus, more related to a more general factor of selective attention and response monitoring. These two factors accounted for 14.4% of the variance in performance on the FAS test.

In sum, we have presented a new methodology that involves determining the main brain areas involved in the task based on data from a meta-analysis to test one of the principles of the STR theory. We have provided support for the idea that individual differences in cognitive abilities may be detected from brain activity at rest by studying the FC between the main areas involved in the task. The results show that performance was predicted by the FC between language-specific brain areas and between areas more related to global cognitive functions.

References

Ackermann, H., & Riecker, A. (2004). The contribution of the insula to motor aspects of speech production: A review and a hypothesis. *Brain and Language*, *89*(2), 320–328. http://doi.org/10.1016/S0093-934X(03)00347-X

Alario, F.-X., Chainay, H., Lehericy, S., & Cohen, L. (2006). The role of the supplementary motor area (SMA) in word production. *Brain Research*, *1076*(1), 129–43. http://doi.org/10.1016/j.brainres.2005.11.104

Baldassarre, A., Lewis, C. M., Committeri, G., & Snyder, A. Z. (2012). Individual variability in functional connectivity predicts performance of a perceptual task, *109*(9). http://doi.org/10.1073/pnas.1113148109/-/DCSupplemental.www.pnas.org/cgi/doi/10.1073/pnas.1113148109

Barttfeld, P., Wicker, B., McAleer, P., Belin, P., Cojan, Y., Graziano, M., … Sigman, M. (2013). Distinct patterns of functional brain connectivity correlate with objective performance and subjective beliefs. *Proceedings of the National Academy of Sciences of the United States of America*, *110*(28), 11577–82. http://doi.org/10.1073/pnas.1301353110

Biswal, B., Yetkin, F. Z., Haughton, V. M., & Hyde, J. S. (1995). Functional connectivity in the motor cortex of resting human brain using echo-planar MRI. *Magnetic Resonance in Medicine*, *34*(4), 537–41. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/8524021

Bookheimer, S. (2002). Functional MRI of language: new approaches to understanding the cortical organization of semantic processing. *Annual Review of Neuroscience*, *25*, 151–88. http://doi.org/10.1146/annurev.neuro.25.112701.142946

Broca P (1861): Remarques sur le siege de la faculte du langage articule; suivies d'une observation d'aphemie (perte de la pa- role): Bull Mem Soc Anat Paris 36:330–357.

Brown, S., Laird, A. R., Pfordresher, P. Q., Thelen, S. M., Turkeltaub, P., & Liotti, M. (2009). The somatotopy of speech: Phonation and articulation in the human motor cortex. *Brain and Cognition*, *70*(1), 31–41. http://doi.org/10.1016/j.bandc.2008.12.006

Costafreda, S. G., Fu, C. H., Picchioni, M., Toulopoulou, T., McDonald, C., Kravariti, E., … McGuire, P. K. (2011). Pattern of neural responses to verbal fluency shows diagnostic specificity for schizophrenia and bipolar disorder. *BMC Psychiatry*, *11*(1), 18. http://doi.org/10.1186/1471-244X-11-18

Costafreda, S. G., Fu, C. H. Y., Lee, L., Everitt, B., Brammer, M. J., & David, A. S. (2006). A systematic review and quantitative appraisal of fMRI studies of verbal fluency: role of the left inferior frontal gyrus. *Human Brain Mapping*, *27*(10), 799–810. http://doi.org/10.1002/hbm.20221

Coste, C. P., Sadaghiani, S., Friston, K. J., & Kleinschmidt, A. (2011). Ongoing brain activity fluctuations directly account for intertrial and indirectly for intersubject variability in Stroop task performance. *Cerebral Cortex (New York, N.Y. : 1991)*, *21*(11), 2612–9. http://doi.org/10.1093/cercor/bhr050

De Luca, M., Smith, S., De Stefano, N., Federico, A., & Matthews, P. M. (2005). Blood oxygenation level dependent contrast resting state networks are relevant to functional activity in the neocortical sensorimotor system. *Experimental Brain Research*, *167*(4), 587–594. http://doi.org/10.1007/s00221-005-0059-1

Demonet, Fiez, Paulesu, Petersen, & Zatorre. (1996). PET Studies of Phonological Processing: A Critical Reply to Poeppel. *Brain and Language*, *55*(3), 352–79. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/8954604

Fox, M. D., Snyder, A. Z., Vincent, J. L., Corbetta, M., Van Essen, D. C., & Raichle, M. E. (2005). The human brain is intrinsically organized into dynamic, anticorrelated functional networks. *Proceedings of the National Academy of Sciences of the United States of America*, *102*(27), 9673–8. http://doi.org/10.1073/pnas.0504136102

Friston, K. (2009). Causal modelling and brain connectivity in functional magnetic resonance imaging. *PLoS Biology*, *7*(2), 0220–0225. http://doi.org/10.1371/journal.pbio.1000033

Gauthier, C. T., Duyme, M., Zanca, M., & Capron, C. (2009). Sex and performance level effects on brain activation during a verbal fluency task: a functional magnetic resonance imaging study. *Cortex; a Journal Devoted to the Study of the Nervous System and Behavior*, *45*(2), 164–76. http://doi.org/10.1016/j.cortex.2007.09.006

Hampshire, A., Chamberlain, S. R., Monti, M. M., Duncan, J., & Owen, A. M. (2010). The role of the right inferior frontal gyrus: inhibition and attentional control. *NeuroImage*, *50*(3), 1313–1319. http://doi.org/10.1016/j.neuroimage.2009.12.109

Harmelech, T., & Malach, R. (2013). Neurocognitive biases and the patterns of spontaneous correlations in the human cortex. *Trends in Cognitive Sciences*, *17*(12), 606–15. http://doi.org/10.1016/j.tics.2013.09.014

Heim, S., Eickhoff, S. B., & Amunts, K. (2008). Specialisation in Broca's region for semantic, phonological, and syntactic fluency? *NeuroImage*, *40*(3), 1362–8. http://doi.org/10.1016/j.neuroimage.2008.01.009

Henry, J. D., & Crawford, J. R. (2004). A Meta-Analytic Review of Verbal Fluency Performance Following Focal Cortical Lesions. *Neuropsychology*, *18*(2), 284–295. http://doi.org/10.1037/0894-4105.18.2.284

Hirshorn, E. a, & Thompson-Schill, S. L. (2006). Role of the left inferior frontal gyrus in covert word retrieval: neural correlates of switching during verbal fluency. *Neuropsychologia*, *44*(12), 2547–57. http://doi.org/10.1016/j.neuropsychologia.2006.03.035

Holmes, G. (1917). The symptoms of acute cerebellar injures due to gunshot injuries. *Brain*, *40*(4), 461–535. http://doi.org/10.1093/brain/40.4.461

Indefrey, P., & Levelt, W. J. M. (n.d.). The Neural Correlates of Language Production. *Language Production*, 845–865.

Lewis, C. M., Baldassarre, A., Committeri, G., Romani, G. L., & Corbetta, M. (2009). Learning sculpts the spontaneous activity of the resting human brain. Supporting Information. *Proceedings of the National Academy of Sciences of the United States of America*, *106*(41), 17558–63. http://doi.org/10.1073/pnas.0902455106

Lezak, M.D., 1995. Neuropsychological Assessment (3rd ed.) New York: Oxford University Press.

Lezak, M. D., Howieson, D. B., Bigler, E. D., & Tranel, D. (2012). Neuropsychological assessment (5th ed.). New York: Oxford University Press

Llano, D. A. (2013). Functional imaging of the thalamus in language. *Brain and Language*, *126*(1), 62–72. http://doi.org/10.1016/j.bandl.2012.06.004

Lowe, M. J., Mock, B. J., & Sorenson, J. A. (1998). Functional Connectivity in Single and Multislice Echoplanar Imaging Using Resting-State Fluctuations. *NeuroImage*, *7*(2), 119–132. http://doi.org/10.1006/nimg.1997.0315

Maldjian, J. A., Laurienti, P. J., Kraft, R. A., & Burdette, J. H. (2003). An automated method for neuroanatomic and cytoarchitectonic atlas-based interrogation of fMRI data sets. *NeuroImage*, *19*(3), 1233–9. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/12880848

Martin, A., Barnes, K. A., & Stevens, W. D. (2012). Spontaneous neural activity

predicts individual differences in performance. *Proceedings of the National Academy of Sciences of the United States of America*, *109*(9), 3201–2. http://doi.org/10.1073/pnas.1200329109
Mazaika, P., Whitfield-Gabrieli, S., & Reiss, A. (2007) Artifact Repair for fMRI Data from High Motion Clinical Subjects. Human Brain Mapping Conference.
Mennes, M., Kelly, C., Zuo, X.-N., Di Martino, A., Biswal, B. B., Castellanos, F. X., & Milham, M. P. (2010). Inter-individual differences in resting-state functional connectivity predict task-induced BOLD activity. *NeuroImage*, *50*(4), 1690–701. http://doi.org/10.1016/j.neuroimage.2010.01.002
Nir, Y., Hasson, U., Levy, I., Yeshurun, Y., & Malach, R. (2006). Widespread functional connectivity and fMRI fluctuations in human visual cortex in the absence of visual stimulation. *NeuroImage*, *30*(4), 1313–1324. http://doi.org/10.1016/j.neuroimage.2005.11.018
Palomar-García, M.-Á., Zatorre, R. J., Ventura-Campos, N., Bueichekú, E., & Ávila, C. (2016). Modulation of Functional Connectivity in Auditory–Motor Networks in Musicians Compared with Nonmusicians. Cerebral Cortex, bhw120. http://doi.org/10.1093/cercor/bhw120
Patterson, J. (2011). F-A-S Test. In J. Kreutzer, J. DeLuca, & B. Caplan (Eds.), *Encyclopedia of Clinical Neuropsychology SE - 886* (pp. 1024–1026). Springer New York. http://doi.org/10.1007/978-0-387-79948-3_886
Power, J. D., Barnes, K. A., Snyder, A. Z., Schlaggar, B. L., & Petersen, S. E. (2012). Spurious but systematic correlations in functional connectivity MRI networks arise from subject motion. *NeuroImage*, *59*(3), 2142–2154. http://doi.org/10.1016/j.neuroimage.2011.10.018
Price, C. J. (2000). The anatomy of language : contributions from functional neuroimaging, *44*, 335–359.
Price, C. J. (2010). The anatomy of language: A review of 100 fMRI studies published in 2009. *Annals of the New York Academy of Sciences*, *1191*, 62–88. http://doi.org/10.1111/j.1749-6632.2010.05444.x
Price, C. J. (2012). A review and synthesis of the first 20years of PET and fMRI studies of heard speech, spoken language and reading. *NeuroImage*, *62*(2), 816–847. http://doi.org/10.1016/j.neuroimage.2012.04.062
Riecker, A., Ackermann, H., Wildgruber, D., Dogil, G., & Grodd, W. (2000). Opposite hemispheric lateralization effects during speaking and singing at motor cortex, insula and cerebellum. *Neuroreport*, *11*(9), 1997–2000. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/10884059
Robinson, G., Shallice, T., Bozzali, M., & Cipolotti, L. (2012). The differing roles of the frontal cortex in fluency tests. *Brain : A Journal of Neurology*, *135*(Pt 7), 2202–14. http://doi.org/10.1093/brain/aws142
Ruff, R. M., Light, R. H., Parker, S. B., & Levin, H. S. (1997). The Psychological Construct of Word Fluency. *Brain and Language*, *57*(3), 394–405. http://doi.org/10.1006/brln.1997.1755
Satterthwaite, T. D., Wolf, D. H., Loughead, J., Ruparel, K., Elliott, M. A., Hakonarson, H., … Gur, R. E. (2012). Impact of in-scanner head motion on multiple measures of functional connectivity: Relevance for studies of neurodevelopment in youth. *NeuroImage*, *60*(1), 623–632. http://doi.org/10.1016/j.neuroimage.2011.12.063
Saur, D., Kreher, B. W., Schnell, S., Kummerer, D., Kellmeyer, P., Vry, M.-S., … Weiller, C. (2008). Ventral and dorsal pathways for language. *Proceedings of the National Academy of Sciences*, *105*(46), 18035–18040. http://doi.org/10.1073/pnas.0805234105

Senhorini, M. C. T., Cerqueira, C. T., Schaufelberger, M. S., Almeida, J. C., Amaro, E., Sato, J. R., … Busatto, G. F. (2011). Brain activity patterns during phonological verbal fluency performance with varying levels of difficulty: A functional magnetic resonance imaging study in Portuguese-speaking healthy individuals. *Journal of Clinical and Experimental Neuropsychology*, *33*(8), 864–873. http://doi.org/10.1080/13803395.2011.561299

Spreen, O., & Benton, A. L. (1977). *Neurosensory Center Comprehensive Examination for Aphasia*. Victoria BC: University of Victoria, Neuropsychology Laboratory.

Stoodley, C., & Schmahmann, J. (2009). Functional topography in the human cerebellum: A meta-analysis of neuroimaging studies. *NeuroImage*, *44*(2), 489–501. http://doi.org/10.1016/j.neuroimage.2008.08.039

Van Dijk, K. R. A., Sabuncu, M. R., & Buckner, R. L. (2012). The influence of head motion on intrinsic functional connectivity MRI. *NeuroImage*, *59*(1), 431–438. http://doi.org/10.1016/j.neuroimage.2011.07.044

Ventura-Campos, N., Sanjuán, A., González, J., Palomar-García, M.-Á., Rodríguez-Pujadas, A., Sebastián-Gallés, N., … Ávila, C. (2013). Spontaneous brain activity predicts learning ability of foreign sounds. *The Journal of Neuroscience : The Official Journal of the Society for Neuroscience*, *33*(22), 9295–305. http://doi.org/10.1523/JNEUROSCI.4655-12.2013

Wagner, S., Sebastian, A., Lieb, K., Tüscher, O., & Tadić, A. (2014). A coordinate-based ALE functional MRI meta-analysis of brain activation during verbal fluency tasks in healthy control subjects. *BMC Neuroscience*, *15*, 19. http://doi.org/10.1186/1471-2202-15-19

Wang, X., Han, Z., He, Y., Caramazza, A., Song, L., & Bi, Y. (2013). Where color rests: spontaneous brain activity of bilateral fusiform and lingual regions predicts object color knowledge performance. *NeuroImage*, *76*, 252–63. http://doi.org/10.1016/j.neuroimage.2013.03.010

Weiss, E. (2003). Brain activation pattern during a verbal fluency test in healthy male and female volunteers: a functional magnetic resonance imaging study. *Neuroscience Letters*, *352*, 191–194. http://doi.org/10.1016/S0304-3940(03)01076-0

Weiss, E. M., Hofer, A., Golaszewski, S., Siedentopf, C., Brinkhoff, C., Kremser, C., … Fleischhacker, W. W. (2004). Brain activation patterns during a verbal fluency test-a functional MRI study in healthy volunteers and patients with schizophrenia. *Schizophrenia Research*, *70*(2-3), 287–91. http://doi.org/10.1016/j.schres.2004.01.010

Yan C and Zang Y (2010) DPARSF: a MATLAB toolbox for "pipeline" data analysis of resting-state fMRI. Front. Syst. Neurosci. 4:13. doi:10.3389/fnsys.2010.00013

Zou, Q., Ross, T. J., Gu, H., Geng, X., Zuo, X.-N., Hong, L. E., … Yang, Y. (2013). Intrinsic resting-state activity predicts working memory brain activation and behavioral performance. *Human Brain Mapping*, *34*(12), 3204–15. http://doi.org/10.1002/hbm.22136