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White matter structures associated with creativity: Evidence from diffusion tensor imaging

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ABSTRACT

Creativity has been essential to the development of human civilization and plays a crucial role in cultural life. However, despite literature that has proposed the importance of structural connectivity in the brain for creativity, the relationship between regional white matter integrity and creativity has never been directly investigated. In this study, we used diffusion tensor imaging and a behavioral creativity test of divergent thinking to investigate the relationship between creativity and structural connectivity. We examined associations between creativity and fractional anisotropy across the brain in healthy young adult (mean age, 21.7 years old; [SD] = 1.44) men ($n = 42$) and women ($n = 13$). After controlling for age, sex, and score on Raven's advanced progressive matrices, a test for psychometric measures of intelligence, significant positive relationships between fractional anisotropy and individual creativity as measured by the divergent thinking test were observed in the white matter in or adjacent to the bilateral prefrontal cortices, the body of the corpus callosum, the bilateral basal ganglia, the bilateral temporo-parietal junction and the right inferior parietal lobule. As a whole, these findings indicate that integrated white matter tracts underlie creativity. These pathways involve the association cortices and the corpus callosum, which connect information in distant brain regions and underlie diverse cognitive functions that support creativity. Thus, our results are congruent with the ideas that creativity is associated with the integration of conceptually distant ideas held in different brain domains and architectures and that creativity is supported by diverse high-level cognitive functions, particularly those of the frontal lobe.

Introduction

Creativity is commonly agreed to involve bringing something into being that is original and valuable (Ochse, 1990). Creativity has been essential to the development of human civilization and plays a crucial role in cultural life. Divergent thinking has been proposed to be a key aspect of creativity (Guilford, 1967). Divergent thinking pertains primarily to information retrieval and the call for a number of varied responses to a certain item (Guilford, 1967). A meta-analysis (Kim, 2008) demonstrated that divergent-thinking scores have a significantly stronger relationship with creative achievement than do scores on intelligence tests, supporting the validity of divergent thinking as predictor of creative ability.

Previous neuropsychological and imaging studies have indicated that inter- and intrahemispheric connectivity as well as the frontal lobe play a key role in creativity. For example, a previous electroencephalogram (EEG) study (Jausovec, 2000) reported that creative individuals had more inter- and intrahemispheric EEG coherence than those who were less creative during an open-ended task (essay writing). Furthermore, the total size of the corpus callosum, an essential component of interhemispheric communication, was associated with creativity as measured by a divergent thinking test (Moore et al., 2009). An fMRI study reported that, during a task that taps divergent thinking, the right prefrontal cortex showed significant activation when participants were asked to create stories in response to the presentation of unrelated words (Howard-Jones et al., 2005). A near-infrared spectroscopy (NIRS) study of divergent thinking (Folley and Park, 2005) found a bilateral increase in frontal activity when participants were engaged in generating novel uses for common objects (divergent thinking). These reports are consistent with the integrative reviews of creativity studies (based on other research methods on creativity such as lesion studies, studies involving cognitive tests, pharmacological interventions and physiological measures) which suggested that structural connectivity in the frontal lobe and white matter, particularly that of the corpus callosum, serves as the neural basis underlying creativity (Flaherty, 2005,

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Heilman et al., 2003, Bogen, 2000). Structural connectivity imaging provides productive and direct answers to these long-suggested views about the structural basis underlying creativity without being sensitive to the specific task demands of the mental task used during the imaging protocol, unlike functional imaging studies.

However, despite the vast amount of literature on creativity, no previous study has observed the relationship between structural integrity in white matter and individual creativity. In this study, we focus on this unresolved issue using tests of divergent thinking and structural connectivity analyses of voxel by voxel fractional anisotropy (FA) in diffusion tensor imaging (DTI) (Le Bihan, 2003). In DTI, FA in each voxel was used as a measure of structural integrity (Chua et al., 2008). Given the previous neuroscientific studies on creativity that indicated the association between creativity, the frontal lobe, and inter- and intrahemispheric connectivity as described above, we reasoned that increased integrity in the structural connections of the frontal lobe and the corpus callosum would be associated with individual creativity as measured by the divergent thinking test.

Methods

Subjects

Fifty-five healthy, right-handed individuals (42 men and 13 women) participated in this study as part of our ongoing project to investigate the association between brain imaging, cognitive function and aging. All the subjects who took part in this study also became the subjects of our intervention studies, and they underwent psychological tests as well as MRI scans that are that are not described in this study, but were performed together with those that are described in this study. The mean age was 21.7 years old (standard deviation [SD], 1.44). All the subjects were university students or postgraduate students. Most of the subjects belong to Tohoku University. They were recruited using adverts on bulletin boards at Tohoku University or by introducing the study by e-mail to subjects of our laboratory's previous experiments. All the subjects had normal vision and no history of neurological or psychiatric illnesses. Handedness was evaluated using the Edinburgh Handedness Inventory (Oldfield, 1971). Written informed consent for all the studies in which the subjects participated was obtained. The procedures of all studies were approved by the Ethics Committee of Tohoku University.

Experimental procedure

On the first day of the interventional experiment, a psychological-test session and MRI were performed. The psychological-test session consisted of a face-to-face part and a group part. The face-to-face part involved three tests that were irrelevant to this study and it took about 20 min per subject. During the group part, assessment of general intelligence was performed first, and assessment of creativity was performed last, together with several other tests (irrelevant to this study) performed between the two tests. The group part took about 2 h. During MRI experiments, there were two sessions. During the first MRI session, the first fMRI scans (mental calculation), T1-weighted image and arterial spin labeling image were obtained in this order. It took about 20 min. During the second session, the second fMRI scans (working memory) and diffusion-weighted image were obtained in this order. It took about 30 min. Subjects also completed a few questionnaires that were not used in this study while they waited for the next procedure.

Creativity assessment

The S-A creativity test (Society for Creative Mind, 1969) was used to assess creativity. J.P. Guilford formed the draft plan and supervised the development of the test, after which the test was standardized for Japanese speakers (Society for Creative Mind, 1969). A more detailed discussion of the psychometric properties of this instrument and how it was developed can be found in the technical manual of this test (Society for Creative Mind, 1969). The test is used to evaluate creativity through divergent thinking (Society for Creative Mind, 1969) and it involves three types of task. Each task is preceded by two minutes of practice involving two questions with a five-minute time limit. All the participants answer the same questions. The first task requires subjects to generate unique ways of using typical objects (e.g., 'Other than reading, how can we use newspapers? An example answer is 'We can use them to wrap things'). The second task requires subjects to imagine desirable functions of ordinary objects (e.g., 'What are the characteristics of a good TV? Write down as many characteristics as possible.' An example answer is 'A TV that can receive broadcasts from all over the world'). The third task requires subjects to imagine the consequences of 'unimaginable things' happening (e.g., 'What would happen if all the mice in the world disappeared?' An example answer is 'The world would become more hygienic'). Each task requires subjects to generate as many answers as possible. The S-A creativity test has two versions: Version A and Version C. Each version has the same three types of task, but involves different questions. The newest version of this test is Version C, which was published in 1993. There was a Version B, together with Version A, in this test, but one question in Version B included one out-of-date item, so it was replaced by Version C. It has been a long time since Version A was published, but the problems in Version A are still not outdated. Therefore, now only Version A and Version C are available. These versions are interchangeable. Therefore, these two versions can be used to investigate the effects of the intervention in interventional studies. In this study, Version A was used.

This test provides a total creativity score, which was used in this study and scores the following dimensions of the creative process: (a) Fluency – Fluency is measured by the number of relevant responses and is related to the ability to produce and consider many alternatives. Fluency scoring is measured by the total number of answers after excluding inappropriate answers or answers that are difficult to understand. (b) Flexibility – Flexibility is the ability to produce responses from a wide perspective. Flexibility scoring is measured by the sum of the (total) number of category types to which answers are assigned on the basis of a criteria table or an almost equivalent judgment. The criteria table is a table that determines what score should be given to certain answers and what category certain answers belong to. However, graders must judge how much score should be given or what category certain answers belong to when the answer is not in listed in the table. Their judgment is considered to be almost, but not equivalent to the criteria table and the criteria table has superiority. (c) Originality – Originality is the ability to produce ideas that differ from those of others. Originality scoring is based on the sum of the categories that are weighted based on the criteria table or an almost equivalent judgment. Originality is determined by the criteria table. The table determines what score should be given to answers of certain category. In the criteria table, how much score should be given is determined on the basis of how rare the category of certain answers is. (d) Elaboration – Elaboration is the ability to produce ideas in detail (Society for Creative Mind, 1969). Elaboration scoring is measured by the sum of the answers that are weighted based on the criteria table or an almost equivalent judgment. These four dimensions correspond to the same concepts as in the Torrance tests of creative thinking (TTCT; Torrance, 1966). The total creativity score is the sum of the raw score of originality and that of elaboration in Version A of the S-A creativity test. This is because the scores for Fluency and Flexibility are highly correlated with that for Elaboration (Society for Creative Mind, 1969). Scoring of the tests was performed at Tokyo Shinri Corporation.

Scores of the S-A creativity test have been shown to be significantly correlated with various other external measures such as various personality factors and problem solving abilities in daily life, suggesting its ability to predict performance in everyday situations (Shimonaka and Nakazato, 2007). Furthermore, scores of the S-A creativity test have been shown to be significantly correlated with frequency of visual hypnagogic experiences which in turn correlated with the vividness of mental imagery and neuroticism (Watanabe, 1998).

Assessment of general intelligence

Raven's Advanced Progressive Matrix (RAPM) (Raven, 1998), which is a psychometric measure of general intelligence (Raven, 1998) and which is often shown to be the most correlated with general intelligence (Raven, 1998), was used to assess general intelligence. General intelligence refers to the *g* factor (Spearman, 1904), which contributes to success in diverse form of cognitive tests regardless of whether they are verbal or nonverbal. This test was used in our study to adjust for the relationship between individual psychometric measures of intelligence on brain structures. This adjustment was performed because creativity is known to be correlated with psychometric measures of intelligence among subjects of low to average intelligence (Barron and Harrington, 1981). However, we did not necessarily expect to find a significant correlation between creativity and intelligence in our study because our subjects were all highly educated. This test was also performed to exclude the possibility that any significant correlation between white matter integrity and creativity is caused by the indirect association between white matter integrity and general intelligence, which is broader and more inclusive of other cognitive abilities. The test contains 36 nonverbal items requiring fluid reasoning ability. Each item consists of a 3×3 matrix with a missing piece to be completed by selecting the best of 8 alternatives. The score of this test (number of correct answers in 30 min) was used as a psychometric index of individual intelligence. The RAPM was administered in a group setting in this study. The RAPM tests can be administered individually by a psychologist or trained test administrator, or administered on a group basis (Raven, 1998).

Image acquisition

All MRI data acquisition was conducted with a 3-T Philips Intera Achieva scanner. The diffusion-weighted data were acquired by using a spin-echo EPI sequence (TR = 10293 ms, TE = 55 ms, big delta (Δ) = 26.3 ms, little delta (δ) = 12.2 ms, FOV = 22.4 cm, $2 \times 2 \times 2$ mm^3 voxels, slice thickness = 2 mm, 60 slices, SENSE reduction factor = 2, number of acquisitions = 1). The diffusion weighting was isotropically distributed along 32 directions (*b* value = 1,000 s/mm^2). Additionally, a data set with no diffusion weighting (*b* value = 0 s/mm^2) ($b = 0$ image) was acquired. The total scan time was 7 min 17 s. Fractional anisotropy values were calculated from the collected images.

Preprocessing of diffusion imaging data and statistical analysis

The DTI signal reflects the mean water diffusion rate in several unique directions. Such information is of particular interest for making inferences about the microstructural properties of white matter, since diffusion is faster along axons than it is in the perpendicular direction. The main barrier is presumably the axonal membrane itself, with the myelin sheath giving rise to additional hindrance. Diffusion in white matter is thus anisotropic, i.e., the diffusion rates in different directions are unequal; isotropic diffusion, in contrast, is equally fast in all directions. Fractional anisotropy (FA) in each voxel was used as a measure of the degree of diffusion anisotropy, with FA reflecting the angle (degree of directionality) of cellular structures within the fiber tracts and therefore structural integrity (Chua et al., 2008). FA varies between 0, representing isotropic diffusion, and 1, in the case of the diffusion taking place entirely in one direction.

Preprocessing and data analysis were performed using statistical Parametric Mapping software (SPM5; Wellcome Department of Cognitive Neurology, London, UK) implemented in Matlab (Mathworks Inc., Natick, MA, USA). Prior to normalization of the FA map, an original skull-stripped $b = 0$ image template was created as follows. (1) The skull of the unsmoothed $b = 0$ images of all the subjects in this study was stripped by masking the images using the threshold of a given signal intensity from spatially smoothed (using 8 mm FWHM) $b = 0$ images of each participant. The threshold to perform the skull stripping was the same for all the subjects and it was determined by visual inspection so that the skulls of the subjects were stripped but the brain parenchymas of the subjects were not deleted. The first smoothing for skull stripping was performed to make mask images for skull stripping the unsmoothed $b = 0$ images, the processed $b = 0$ images that go to the next processing step are unsmoothed images. (2) Then, this skull-stripped unsmoothed $b = 0$ image was spatially normalized to the skull-stripped T2 template in SPM5. (3) The normalized skull-stripped $b = 0$ image was then smoothed using a Gaussian kernel of 8 mm FWHM and finally averaged.

Then, the skull-stripped $b = 0$ image of each participant was normalized to our original skull-stripped $b = 0$ image template. Using the parameters for this normalizing procedure, the FA map image of each participant was spatially normalized to create images with 2-* 2- * 2-mm^3 voxels. Non-white matter tract parts of normalized images were omitted from the normalized images before the spatial filtering operation to avoid the possibility that FA differences outside white matter tracts affect the FA value inside WM tracts after spatial smoothing. This was done by masking normalized unsmoothed FA images with normalized skull-stripped unsmoothed $b = 0$ images (that were described above) (to omit the non-brain parenchyma voxels) and also omitting the voxels of FA value <0.25 from normalized FA images. Then, these processed normalized images were spatially smoothed using a Gaussian kernel of 12 mm FWHM. The resulting maps representing the FA were then forwarded to the group regression analysis described below.

At the group level analysis, we tested for a relationship between individual creativity and regional FA. In the whole brain analysis, we used a multiple linear regression analysis to look for areas where the FA was significantly related to individual creativity measured by the divergent thinking test (total creativity score in the S-A creativity test). The analysis was limited to total creativity score and did not include the score of each dimension because the score of each dimension highly correlated with total creativity score (each correlation efficient >0.79). Consistent with this, a previous study (Chávez-Eakle et al., 2007) that investigated the association between regional cerebral flow (rCBF) and each dimension revealed that different creativity dimensions correlated with rCBF in similar regions. Thus, we believe that using only the total creativity score serves the purpose of this study. We did not use each dimension as usually performed in the case of studies of the relationship between brain structure and psychometric measures of intelligence that do not focus on specific cognitive faculties but focus on general intellectual ability (e.g., Haier et al., 2004). The analysis was performed with sex, age and the score of RAPM as additional covariates. All tests on fractional anisotropy were performed using an absolute threshold of FA >0.2 (Albrecht et al., 2007), such that if a voxel anywhere in the brain had an FA value of more than 0.2 in all the subjects, that voxel is included in the analysis. This measure was taken because FA is more susceptible to error arising from partial volumes (Pfefferbaum and Sullivan, 2003), and with this FA cutoff value we can dissociate white matter structure from other tissues (Salat et al., 2005). We can also dissociate the white matter structures of large bundles that connect different brain regions such as the corpus callosum, as described in the Introduction, from other tissues with this value.

Multiple comparison correction was performed using the false discovery rate (FDR) approach (Genovese et al., 2002). The FDR approach was applied within areas that showed FA value >0.20 across the whole brain. FDR-based methods have been shown to be more powerful and sensitive than other available approaches to multiple statistical testing (see Genovese et al., 2002; Benjamini and Hochberg, 1995 for a full discussion). In FDR testing, if there is truly no signal (non-noise) anywhere in the brain, an FDR-controlling method has the same control as family-wise error correction. That is, if the null hypothesis is true everywhere, an FDR procedure will control the chance of a false positive anywhere in the brain at a specified level (Benjamini and Hochberg, 1995). In fact, in an actual data set that is not expected to contain a true signal, FDR correction becomes more conservative than family-wise error correction (Meyer-Lindenberg et al., 2008).

The anatomical label of nearest gray matter area of voxels in the table was determined by using Talairach Daemon (TD) Labels of Wake Forest University (WFU) Pickatlas (http://www.fmri.wfubmc.edu/download.htm). The anatomical label of "lobe" in the table was determined using WFU Pickatlas's TD Lobes. In other parts of the text, regions were determined using these labels (such as the frontal lobe, inferior parietal lobule, occipital lobe and corpus callosum), or a combination of anatomical definition and these labels (such as the striatum which consists of putamen and caudate), or visual inspection based on previous literatures (such as the temporo-parietal junction).

Results

Behavioral data

Table 1 shows the demographic statistics of males and females across total S-A creativity test score, age and RAPM score. Behavioral data revealed an average total S-A creativity test score of 37.42 (SD, 11.49; range, 14–67) and an average RAPM score of 28 (SD, 3.42; range, 23–34). None of the psychological and epidemiological measures (RAPM score, age or sex) correlated significantly with the total S-A creativity test score. For complete data of the distribution of the total S-A creativity test score, see Fig. 1.

Correlation of FA and creativity

Total score of the S-A creativity test significantly and positively correlated with FA throughout a large part of the white matter regions in the frontal lobe and the anterior cingulate cortex bilaterally (Fig. 2A), extending into the body of the corpus callosum (Fig. 2B), white matter regions in and adjacent to the bilateral striatum (Fig. 2C) as well as white matter regions adjacent to the bilateral temporo-parietal junction and a white matter region extending into the right temporo-parietal junction from the frontal lobe (arcuate fasciculus) (Fig. 2D). Furthermore, there was a significant positive correlation between the FA and the total score of the S-A creativity test in white matter regions adjacent to the anterior part of the bilateral inferior parietal lobule (IPL) (supramarginal gyrus) (the left one is shown in Fig. 2E) and in a white matter region in the right occipital lobe (Fig. 2F). These results are shown in Table 2.

Table 1
Demographic variables for the sample of males and females.

Measure	Males		Females	
	Mean	SD	Mean	SD
Age	21.67	1.51	21.85	1.21
RAPM	27.93	3.31	28.23	3.90
S-A creativity test	36.29	12.08	41.08	8.77

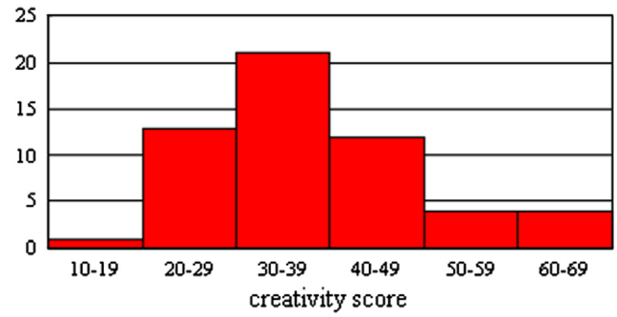

Fig. 1. Distribution of the scores from the S-A creativity test in our sample.

These results are not significantly affected by including the score of RAPM as a covariate, since all the significant results above remained significant after excluding the score of RAPM.

Discussion

To the best of our knowledge, this is the first study to investigate the association between individual creativity and white matter integrity as measured by diffusion tensor imaging. Consistent with our hypothesis, our findings showed that increased integrity in structural connectivity involving the frontal lobe and the corpus callosum was significantly and positively correlated with individual creativity as measured by the divergent thinking test. Furthermore, a significant correlation was found in white matter regions adjacent to the bilateral striatum, the right temporo-parietal junction, the anterior part of the bilateral IPL and the right occipital lobe. As a whole, these findings are congruent with the long-held ideas that creativity is associated with (1) 'efficient integration of information' through integrated white matter pathways (particularly those of the frontal lobe and the corpus callosum) as well as (2) 'diverse high-level cognitive functions' (those of diverse brain areas but particularly those of the frontal lobe), which are facilitated by regionally integrated white matter pathways.

Consistent with our hypothesis, a significant positive correlation between white matter integrity (FA) and creativity was found in the white matter regions of the frontal lobe, which have many functions that are associated with creativity. Creativity is a complex cognitive function that requires diverse cognitive abilities, such as working memory, sustained attention, cognitive flexibility, and fluency in the generation of ideas and in the judgment of propriety, which are typically ascribed to the prefrontal cortex (Dietrich, 2004, Baldo et al., 2001). For example, cognitive flexibility, or the ability to break conventional or obvious patterns of thinking to adopt new and higher-order rules, is at the heart of creativity theories such as Guilford's (1967) concept of divergent thinking. White matter integrity (FA) in the frontal lobe is positively correlated with subcomponents of creativity such as working memory and fluency (Olesen et al., 2003; O'Sullivan et al., 2001). Any disruptions in the pathways of the frontal lobe may impair the execution of frontal lobe functions (Moseley et al., 2002). Thus, one possible mechanism that underlies the correlation between white matter integrity and creativity, which was found in our results, is the extent to which increased structural integrity in the frontal lobe supports high-level frontal lobe cognitive functions, which in turn contribute to improved creativity.

Significant positive correlation between white matter integrity (FA) and creativity was found in the white matter regions extending into and adjacent to the bilateral striatum, which through the regulation of the dopaminergic system underlies some of the creativity-related high-level cognitive functions. The striatum receives abundant projections from the frontal lobe (Alexander et al., 1986; Middleton and Strick, 2000, 2002) and the dopaminergic system plays

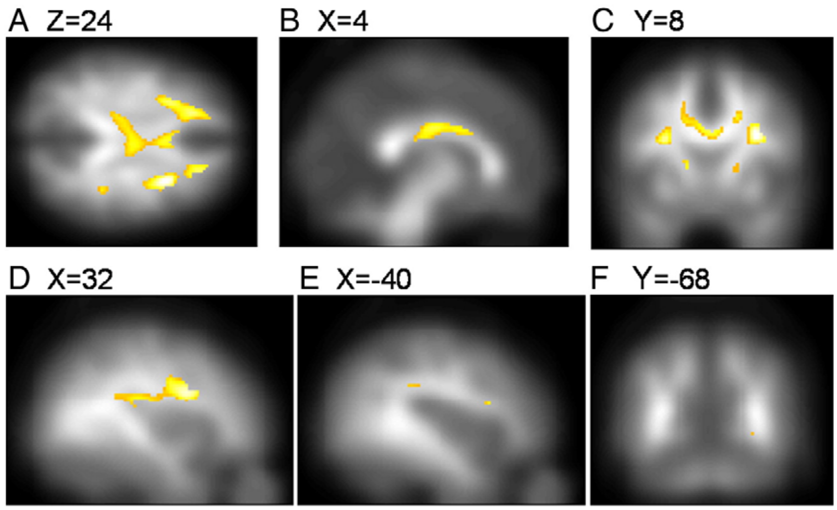

Fig. 2. Regions of correlation between FA and the scores in the creativity test ($p<0.05$, corrected for FDR with an extent threshold of 20 voxels). Regions of significant correlation are overlaid on the mean, smoothed FA images from all participants. (A) Axial view. Regions with significant correlations are shown in the bilateral frontal and anterior cingulate regions together with other regions. (B) Sagittal view. Regions with significant correlations are shown in the corpus callosum. (C) Coronal view. Regions with significant correlations are shown in the regions in and adjacent to the bilateral striatum, together with other regions. (D, E) Sagittal views. (D) Regions with significant correlations are shown in the regions extending from the frontal lobe into the right temporo-parietal junction (arcuate fasciculus). (E) Regions with significant correlations are shown in the region adjacent to the left anterior IPL together with other regions. (F) Coronal view. A region with significant correlation is shown in the right occipital lobe.

a role in the regulation of this corticostriatal (and thalamocortical) loop. The dopaminergic neurons in the midbrain area project close to the corticostriatal glutamatergic synapses (Smith and Bolam, 1990), and are known to modulate corticostriatal connection strength (Bamford et al., 2004). These anatomical corticostriatal substrates that are regulated by the dopaminergic system have an effect on frontal lobe functions (Middleton and Strick, 2002). For example, dopamine neurotransmission strengthens functional connectivity between the frontal lobes and the basal ganglia during cognitive flexibility tasks (Nagano-Saito et al., 2008), which are presumed to be associated with creativity, and improves performance in such tasks. Numerous studies have shown that the frontal lobe and striatum are associated with cognitive flexibility (Monchi et al., 2001, 2004, Eslinger and Grattan, 1993, also for review, see Ragozzino, 2007). Furthermore, structural connectivity underlies increased functional connectivity between brain regions (Greicius et al., 2009) and it has been implicated that higher individual white matter integrity underlies stronger functional connectivity (Au Duong et al., 2005). Considering these

Table 2
Brain regions with significant positive correlations between FA values and the scores from the S-A creativity test.

Lobe	Nearest gray matter area		*x*	*y*	*z*	*T* score	Corrected *p* value (FDR)	Cluster size (mm^3)
Frontal lobe	Subgyral	R	28	8	24	4.82	0.019	28,648
Frontal lobe	Subgyral	L	−30	12	20	4.65	0.019	
Sublobar	Extra-nuclear	L	−28	−40	10	4.56	0.019	
Frontal lobe	Medial frontal gyrus	R	22	36	22	4.07	0.020	
Frontal lobe	Subgyral	L	−22	28	26	4.05	0.020	
Limbic lobe	Cingulate gyrus	R	18	2	38	3.73	0.024	
Limbic lobe	Anterior cingulate	L	−2	8	26	3.65	0.025	
Limbic lobe	Cingulate gyrus	R	6	−12	28	3.64	0.025	
Frontal lobe	Subgyral	R	22	44	0	3.58	0.027	
Frontal lobe	Subgyral	R	24	24	36	3.34	0.030	
Frontal lobe	Subgyral	R	22	22	32	3.27	0.031	
Sublobar	Caudate	R	22	−36	16	3.27	0.031	
Limbic lobe	Cingulate gyrus	R	18	16	34	3.24	0.031	
Limbic lobe	Cingulate gyrus	L	−16	4	34	3.24	0.031	
Sublobar	Insula	R	30	−28	18	3.22	0.032	
Limbic lobe	Cingulate gyrus	R	16	10	34	3.20	0.032	
Parietal lobe	Subgyral	R	36	−40	22	3.14	0.033	
Frontal lobe	Subgyral	L	−16	24	44	3.12	0.033	
Sublobar	Insula	R	32	−18	18	3.11	0.033	
Frontal lobe	Subgyral	L	−18	14	42	2.88	0.039	
Frontal lobe	Subgyral	L	−8	18	24	2.84	0.040	
Frontal lobe	Medial frontal gyrus	R	16	4	52	2.78	0.042	
Sublobar	Extra-nuclear	R	16	14	2	3.40	0.029	616
Sublobar	Lentiform nucleus	L	−16	8	4	3.26	0.031	248
Parietal lobe	Postcentral gyrus	R	44	−26	32	3.13	0.033	136
Parietal lobe	Inferior parietal lobule	L	−40	−36	28	2.80	0.042	56
Parietal lobe	Subgyral	R	26	−56	28	2.76	0.043	64
Frontal lobe	Medial Frontal gyrus	L	−14	2	54	2.71	0.045	80
Occipital lobe	Lingual gyrus	R	24	−72	−4	2.70	0.045	8
Occipital lobe	Lingual gyrus	R	26	−68	−4	2.64	0.048	16

No regions showed significantly negative correlations between FA and the scores from the S-A creativity test. The anatomical label of nearest gray matter area in the table was determined by using Wake Forest University (WFU) Pickatlas's Talairach Daemon (TD) Labels. The anatomical label of "lobe" in the table was determined using WFU Pickatlas's TD Lobes.

points, increased corticostriatal white matter integrity may increase corticostriatal functional connectivity, and lead to improved creativity-related high-level frontal lobe cognitive functions (such as cognitive flexibility) under the regulation of dopamine.

The resulting significant positive correlation between creativity and white matter integrity (FA) in the corpus callosum supports the long-standing view that efficient information integration between the two hemispheres is crucial for creativity. The body of the corpus callosum connects the superior frontal regions (De Lacoste et al., 1985), as well as motor, sensory and auditory cortices (Pandya et al., 1986) while corpus callosum white matter integrity facilitates interhemispheric information processing (Schulte et al., 2005). The relationship between the integrity of this interhemispheric architecture and creativity measured by the divergent thinking test as shown in our results, is consistent with previous functional imaging studies that suggest that divergent and creative thinking are characterized by increased cooperation of the two hemispheres (Atchley et al., 1999; Bekhtereva et al., 2000; Carlsson et al., 2000). Also, previous reviews suggested the importance of bihemispheric information transfer in creativity. For example, Heilman et al. (2003) stated that the right and left hemispheres store different forms of cognitive activity, and a possible method of resolving a previously unsolved problem is to see the problem "in a new light." A means of viewing the problem in a new light is to use a different form of knowledge and a different cognitive strategy that might be mediated by the hemisphere opposite the one previously used. The highly integrated corpus callosum is probably involved in this kind of integrative interhemispheric information processing and leads to high individual creativity.

The significant positive correlation between creativity and increased white matter integrity (FA) in the regions adjacent to the temporo-parietal junction as well as the other association cortices as seen in our results, is congruent with the idea that the integration of information is important for creativity. In addition to interhemispheric communication, as stated in the paragraph above, intrahemispheric communication may also be important for creative innovation because widespread connectivity allows creative people to combine the representations of ideas that were previously isolated. This idea of creativity has also been long stated. For example, James (1890) and Spearman (1931) suggested that creativity requires a combination of elements that have little association and are isolated. Furthermore, it was suggested that greater creativity might be achieved by using brain networks, which represent knowledge in one domain to help organize a quite different domain that might, nevertheless, share some attributes (Heilman et al., 2003). The temporo-parietal junction is a multi-modal assimilation area (Rhawn and Joseph 1996) connected with all the sensory cortical areas and is involved in high-order, complex, multisensory perception, integrating information from vision, touch, balance, and spatial orientation (Spence and Frith, 1999). In addition to the temporo-parietal junction, other association cortices that were identified in our analysis, namely the prefrontal cortex and the anterior IPL, also play a key role in the processing of multimodal information (Prabhakaran et al., 2000, Booth et al., 2002). Integrated white matter pathways in the association cortices involved in the integration of information, and also in the bundle that connects these regions (the right arcuate fasciculus), may allow efficient integration of information in the brain regions involved with different domains. These brain regions in turn allow remote and indirect associations that are salient in creativity as described above.

Integrated white matter pathways adjacent to the anterior IPL, where another significant positive correlation between creativity and integrity was observed, may help individual creativity through the high-level cognitive functions of visual imagery and attention. Previous studies have shown the association between creativity and visual imagery (Finke, 1996). Also, IPL together with the occipital lobe is associated with visual imagery synthesis (Yomogida et al., 2004). Thus, one simple interpretation of our results in the bilateral IPL and the occipital lobe is that integrated white matter pathways in these regions underlie clear visual imagery, which helps the imagination in creative thinking. Yet another interpretation is that integrated white matter pathways in the IPL might lead to an integrated attentional system. The IPL is associated with attention system (Macaluso et al., 2000). On the other hand, previous studies suggested that creative people have a broad focus of attention and a greater attentive capacity (for review, see Folley et al., 2003). For example, studies of general attentive capabilities between creative and noncreative subjects show that subjects who exhibit fewer creative traits focus their attention more narrowly (Dykes and McGhie, 1976).

Some of significant correlations between creativity and white matter integrity were found in the right hemisphere only (i.e., arcuate fasciculus and occipital lobe). These results are congruent with the idea that the right hemisphere is specialized for creativity (Bogen and Bogen, 1988; Hoppe, 1988), possibly through the association between creativity and global attention system which is mediated by the right hemisphere (Moore et al., 2009). Nevertheless, the idea of the selective involvement of the right hemisphere with creativity is a matter of debate (Flaherty, 2005). In our study, too, there were nonsignificant results in the left temporal lobe and left occipital lobe which showed correlations between white matter integrity and creativity (corrected for FDR, $P<0.1$). Thus, the superiority of the right, compared with the left, occipital lobe's (or arcuate fasciculus's) influence on creativity was not clear in this study. Future studies with more statistical power may need to investigate the difference of the bilateral hemispheres in involvement with creativity.

Increased FA, which is presumably secondary to increased myelination (Beaulieu, 2002) or increased axonal caliber (Mori and Zhang, 2006), may be associated with enhanced effectiveness in communication between neural circuits, which leads to enhanced creativity. This is due to the following reasons. An action potential spreads faster along myelinated axons than unmyelinated axons (Bloom et al., 1988). In addition, the velocity of conduction of an action potential spread increases with increased myelin thickness in myelinated neuron fibers (Waxman, 1980) and axonal caliber is a determinant of neuronal conduction velocity (Arbuthnott et al., 1980). Faster conduction velocity can facilitate information flow not only by speeding it up but also by allowing for precise temporal coding of high-frequency bursts of neuronal activity (McDonald and Sears, 1970, Swadlow, 1985, Shrager, 1993). Furthermore, integrity in the timing of sequential events in neuronal circuits could lead to more effective cognitive performance (Peters, 2002).

There are a few limitations in this study. First, our approach was limited; we used young healthy subjects with high-level education and although it is not easy to estimate IQ from the score of RAPM with a 30-min time limitation, the average score (28) of RAPM in our sample is apparently higher than average (Raven, 1998). Thus, our interpretations have a certain limitation; however, focusing on highly intelligent subjects was certainly warranted for the purpose of this study, given the correlation between intelligence and creativity among subjects with normal and inferior intelligence (Sternberg, 2005). Creativity tests require diverse cognitive functions including basic ones, and to understand and solve problems in creativity tests, a moderate level of intelligence is apparently necessary. Thus, we certainly had to disentangle the relationship between creativity and intelligence and exclude the effect of intelligence on structural connectivity. Second, the study population is unbalanced toward males and we did not and could not investigate the sex-specific relationship between white matter integrity and creativity. Previous DTI studies have shown differences both in absolute FA values between males and females (Szeszko et al., 2003) and in the relationship of FA values to cognitive function (Schmithorst, 2009). It is possible that the relationship between white matter structure and creativity may differ between females and males. Third, the associations between creative achievement and scores of this test have not been demonstrated in peer reviewed journals, unlike the Torrance Tests of Creative Thinking (TTCT) (for meta-analysis of the associations between creative achievement and TTCT, see Kim, 2008). So it is a limitation in this study. However, the nature of the S-A creativity test is similar to that of the TTCT in that it consists of three problems, which are similar to three problems in the TTCT (Torrance, 1966). In these problems, the subjects are asked to (1) improve a product (list ways to change a certain product so that it will have more desirable characteristics), (2) find interesting and unusual uses for a certain object and (3) list all the consequences should an improbable situation occur (Torrance, 1966).

This is the first study to investigate the association between regional white matter structural integrity and individual creativity. Creativity is a complex, dynamic, multi-integrative process that simultaneously involves perceptual, volitional, cognitive, and emotional processes (Chávez-Eakle et al., 2007) and requires the diverse, high-level cognitive functions of the frontal lobe as well as the diverse brain areas stated above. The significant correlation shown in our results between creativity measured by the divergent thinking test and white matter structural integrity in widespread regions that are involved in information integration and high-level cognitive functions supports these ideas about the basis of creativity. In addition, it has been suggested that highly integrated white matter pathways underlie increased functional connectivity between relevant brain regions and increased functional activation in relevant brain areas (Au Duong et al., 2005, Olesen et al., 2003). Considering these points, our results may explain previously reported correlations between individual creativity and increased functional connectivity or functional activation in the cortex (e.g., Jausovec, 2000, Chávez-Eakle et al., 2007).

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References

Albrecht, J., Dellani, P.R., Muller, M.J., Schermuly, I., Beck, M., Stoeter, P., Gerhard, A., Fellgiebel, A., 2007. Voxel based analyses of diffusion tensor imaging in Fabry disease. Br. Med. J. 78, 964–969.

Alexander, G.E., DeLong, M.R., Strick, P.L., 1986. Parallel organization of functionally segregated circuits linking basal ganglia and cortex. Annu. Rev. Neurosci. 9, 357–381.

Arbuthnott, E.R., Boyd, I.A., Kalu, K.U., 1980. Ultrastructural dimensions of myelinated peripheral nerve fibres in the cat and their relation to conduction velocity. J. Physiol. 308, 125–157.

Atchley, R.A., Keeney, M., Burgess, C., 1999. Cerebral hemispheric mechanisms linking ambiguous word meaning retrieval and creativity. Brain Cogn. 40, 479–499.

Au Duong, M.V., Boulanouar, K., Ibarrola, D., Malikova, I., Confort-Gouny, S., Celsis, P., Pelletier, J., Cozzone, P.J., Ranjeva, J.P., 2005. Altered functional connectivity related to white matter changes inside the working memory network at the very early stage of MS. J. Cereb. Blood Flow Metab. 25, 1245–1253.

Baldo, J.V., Shimamura, A.P., Delis, D.C., Kramer, J., Kaplan, E., 2001. Verbal and design fluency in patients with frontal lobe lesions. J. Int. Neuropsychol. Soc. 7, 586–596.

Bamford, N.S., Zhang, H., Schmitz, Y., Wu, N.P., Cepeda, C., Levine, M.S., Schmauss, C., Zakharenko, S.S., Zablow, L., Sulzer, D., 2004. Heterosynaptic dopamine neurotransmission selects sets of corticostriatal terminals. Neuron 42, 653–663.

Barron, F., Harrington, D.M., 1981. Creativity, intelligence, and personality. Annu. Rev. Psychol. 32, 439–476.

Beaulieu, C., 2002. The basis of anisotropic water diffusion in the nervous system-a technical review. NMR Biomed. 15, 435–455.

Bekhtereva, N.P., Starchenko, M.G., Klyucharev, V.A., Vorob'ev, V.A., Pakhomov, S.V., Medvedev, S.V., 2000. Study of the brain organization of creativity: II. Positron-emission tomography data. Hum. Physiol. 26, 516–522.

Benjamini, Y., Hochberg, Y., 1995. Controlling the false discovery rate: a practical and powerful approach to multiple testing. J. R. Stat. Soc. Ser. B (Methodological) 289–300.

Bloom, F.E., Lazerson, A., Hofstadter, L., 1988. Brain, mind, and behavior. Freeman.

Bogen, J.E., 2000. Split-brain basics: relevance for the concept of one's other mind. J. Am. Acad. Psychoanal. 28, 341–369.

Bogen, J.E., Bogen, G.M., 1988. Creativity and the corpus callosum. Psychiatr. Clin. North Am. 11, 293–301.

Booth, J.R., Burman, D.D., Meyer, J.R., Gitelman, D.R., Parrish, T.B., Mesulam, M.M., 2002. Functional anatomy of intra-and cross-modal lexical tasks. Neuroimage 16, 7–22.

Carlsson, I., Wendt, P.E., Risberg, J., 2000. On the neurobiology of creativity. Differences in frontal activity between high and low creative subjects. Neuropsychologia 38, 873–885.

Chávez-Eakle, R.A., Graff-Guerrero, A., Garc i a-Reyna, J.C., Vaugier, V., Cruz-Fuentes, C., 2007. Cerebral blood flow associated with creative performance: a comparative study. Neuroimage 38, 519–528.

Chua, T.C., Wen, W., Slavin, M.J., Sachdev, P.S., 2008. Diffusion tensor imaging in mild cognitive impairment and Alzheimer's disease: a review. Curr. Opin. Neurol. 21, 83–92.

De Lacoste, M.C., Kirkpatrick, J.B., Ross, E.D., 1985. Topography of the human corpus callosum. J. Neuropathol. Exp. Neurol. 44, 578–591.

Dietrich, A., 2004. The cognitive neuroscience of creativity. Psychon. Bull. Rev. 11, 1011–1026.

Dykes, M., McGhie, A., 1976. A comparative study of attentional strategies of schizophrenic and highly creative normal subjects. Br. J. Psychiatry 128, 50–56.

Eslinger, P.J., Grattan, L.M., 1993. Frontal lobe and frontal-striatal substrates for different forms of human cognitive flexibility. Neuropsychologia 31, 17–28.

Finke, R.A., 1996. Imagery, creativity, and emergent structure. Conscious. Cogn. 5, 381–393.

Flaherty, A.W., 2005. Frontotemporal and dopaminergic control of idea generation and creative drive. J. Comp Neurol. 493, 147–153.

Folley, B.S., Doop, M.L., Park, S., 2003. Psychoses and creativity: is the missing link a biological mechanism related to phospholipids turnover? Prostaglandins, Leukot. Essent. Fat. Acids 69, 467–476.

Folley, B.S., Park, S., 2005. Verbal creativity and schizotypal personality in relation to prefrontal hemispheric laterality: a behavioral and near-infrared optical imaging study. Schizophr. Res. 80, 271–282.

Genovese, C.R., Lazar, N.A., Nichols, T., 2002. Thresholding of statistical maps in functional neuroimaging using the false discovery rate. Neuroimage 15, 870–878.

Greicius, M.D., Supekar, K., Menon, V., Dougherty, R.F., 2009. Resting-state functional connectivity reflects structural connectivity in the default mode network. Cereb. Cortex 19, 72–78.

Guilford, J.P., 1967. The Nature of Human Intelligence. McGraw-Hill Companies.

Haier, R.J., Jung, R.E., Yeo, R.A., Head, K., Alkire, M.T., 2004. Structural brain variation and general intelligence. Neuroimage 23, 425–433.

Heilman, K.M., Nadeau, S.E., Beversdorf, D.O., 2003. Creative innovation: possible brain mechanisms. Neurocase 9, 369–379.

Hoppe, K.D., 1988. Hemispheric specialization and creativity. Psychiatr. Clin. North Am. 11, 303–315.

Howard-Jones, P.A., Blakemore, S.J., Samuel, E.A., Summers, I.R., Claxton, G., 2005. Semantic divergence and creative story generation: an fMRI investigation. Cogn. Brain Res. 25, 240–250.

James, W., 1890. The Principles of Psychology. Holt, New York.

Jausovec, N., 2000. Differences in cognitive processes between gifted, intelligent, creative, and average individuals while solving complex problems: an EEG study. Intelligence 28, 213–237.

Kim, K.H., 2008. Meta-analyses of the relationship of creative achievement to both IQ and divergent thinking test scores. J. Creat. Behav. 42, 106–130.

Le Bihan, D., 2003. Looking into the functional architecture of the brain with diffusion MRI. Nat. Rev. Neurosci. 4, 469–480.

Macaluso, E., Frith, C.D., Driver, J., 2000. Modulation of human visual cortex by crossmodal spatial attention. Science 289, 1206–1208.

McDonald, W.I., Sears, T.A., 1970. The effects of experimental demyelination on conduction in the central nervous system. Brain 93, 583–598.

Meyer-Lindenberg, A., Nicodemus, K.K., Egan, M.F., Callicott, J.H., Mattay, V., Weinberger, D.R., 2008. False positives in imaging genetics. Neuroimage 40, 655–661.

Middleton, F.A., Strick, P.L., 2000. Basal ganglia output and cognition: evidence from anatomical, behavioral, and clinical studies. Brain Cogn. 42, 183–200.

Middleton, F.A., Strick, P.L., 2002. Basal-ganglia 'projections' to the prefrontal cortex of the primate. Cereb. Cortex 12, 926–935.

Monchi, O., Petrides, M., Petre, V., Worsley, K., Dagher, A., 2001. Wisconsin Card Sorting revisited: distinct neural circuits participating in different stages of the task identified by event-related functional magnetic resonance imaging. J. Neurosci. 21, 7733–7741.

Monchi, O., Petrides, M., Doyon, J., Postuma, R.B., Worsley, K., Dagher, A., 2004. Neural bases of set-shifting deficits in Parkinson's disease. J. Neurosci. 24, 702–710.

Moore, D.W., Bhadelia, R.A., Billings, R.L., Fulwiler, C., Heilman, K.M., Rood, K.M.J., Gansler, D.A., 2009. Hemispheric connectivity and the visual-spatial divergent-thinking component of creativity. Brain Cogn. 70, 267–272.

Mori, S., Zhang, J., 2006. Principles of diffusion tensor imaging and its applications to basic neuroscience research. Neuron 51, 527–539.

Moseley, M., Bammer, R., Illes, J., 2002. Diffusion-tensor imaging of cognitive performance. Brain Cogn. 50, 396–413.

Nagano-Saito, A., Leyton, M., Monchi, O., Goldberg, Y.K., He, Y., Dagher, A., 2008. Dopamine depletion impairs frontostriatal functional connectivity during a set-shifting task. J. Neurosci. 28, 3697–3706.

Ochse, R., 1990. Before the Gates of Excellence: The Determinants of Creative Genius. Cambridge University Press.

Oldfield, R.C., 1971. The assessment and analysis of handedness: the Edinburgh inventory. Neuropsychologia 9, 97–113.

Olesen, P.J., Nagy, Z., Westerberg, H., Klingberg, T., 2003. Combined analysis of DTI and fMRI data reveals a joint maturation of white and grey matter in a fronto-parietal network. Cogn. Brain Res. 18, 48–57.

O'Sullivan, M., Jones, D.K., Summers, P.E., Morris, R.G., Williams, S.C.R., Markus, H.S., 2001. Evidence for cortical “disconnection” as a mechanism of age-related cognitive decline. Neurology 57, 632–638.

Pandya, D.N., Seltzer, B., Lepore, F., Ptito, M., Jasper, H.H., 1986. Two hemispheres-one brain: functions of the corpus callosum. Neurol. Neurobiol. 17, 16–18.

Peters, A., 2002. The effects of normal aging on myelin and nerve fibers: a review. J. Neurocytol. 31, 581–593.

Pfefferbaum, A., Sullivan, E.V., 2003. Increased brain white matter diffusivity in normal adult aging: relationship to anisotropy and partial voluming. Magn. Reson. Med. 49, 953–961.

Prabhakaran, V., Narayanan, K., Zhao, Z., Gabrieli, J.D.E., 2000. Integration of diverse information in working memory within the frontal lobe. Nat. Neurosci. 3, 85–90.

Ragozzino, M.E., 2007. The contribution of the medial prefrontal cortex, orbitofrontal cortex, and dorsomedial striatum to behavioral flexibility. Ann. N. Y. Acad. Sci. 1121, 355–375.

Raven, J., 1998. Manual for Raven's Progressive Matrices and Vocabulary Scales. Psychologists Press Oxford, Oxford.

Rhawn, J., Joseph, R., 1996. Neuropsychiatry, Neuropsychology, and Clinical Neuroscience. Lippincott Williams & Wilkins.

Salat, D.H., Tuch, D.S., Greve, D.N., van der Kouwe, A.J.W., Hevelone, N.D., Zaleta, A.K., Rosen, B.R., Fischl, B., Corkin, S., Rosas, H.D., 2005. Age-related alterations in white matter microstructure measured by diffusion tensor imaging. Neurobiol. Aging 26, 1215–1227.

Schmithorst, V.J., 2009. Developmental sex differences in the relation of neuroanatomical connectivity to intelligence. Intelligence 37, 164–173.

Schulte, T., Sullivan, E.V., Muller-Oehring, E.M., Adalsteinsson, E., Pfefferbaum, A., 2005. Corpus callosal microstructural integrity influences interhemispheric processing: a diffusion tensor imaging study. Cereb. Cortex 15, 1384–1392.

Shimonaka, J., Nakazato, K., 2007. Developmental characteristics of creativity from adulthood to old-age and its associated factors. *Kyoikushinrigakukenkyu*. (Educ. Psychol. Res.) 55, 21–243.

Shrager, P., 1993. Axonal coding of action potentials in demyelinated nerve fibers. Brain Res. 619, 278–290.

Smith, A.D., Bolam, J.P., 1990. The neural network of the basal ganglia as revealed by the study of synaptic connections of identified neurones. Trends Neurosci. 13, 259–265.

Society for Creative Mind, 1969. Manual of S-A Creativity Test. Tokyo Shinri Corporation.

Spearman, C., 1904. General intelligence, objectively determined and measured. Am. J. Psychol. 15, 201–293.

Spearman, C.D., 1931. Creative Mind. Macmillan, London.

Spence, S.A., Frith, C.D., 1999. Towards a functional anatomy of volition. J. Conscious. Stud. 68, 11–29.

Sternberg, R.J., 2005. Handbook of Creativity. Cambridge UP, New York.

Swadlow, H.A., 1985. Physiological properties of individual cerebral axons studied in vivo for as long as one year. J. Neurophysiol. 54, 1346–1362.

Szeszko, P.R., Vogel, J., Ashtari, M., Malhotra, A.K., Bates, J., Kane, J.M., Bilder, R.M., Frevert, T., Lim, K., 2003. Sex differences in frontal lobe white matter microstructure: a DTI study. Neuroreport 14, 2469–2473.

Torrance, E.P., 1966. Torrance Tests of Creative Thinking. Scholastic Testing Service Bensenville, Ill.

Yomogida, Y., Sugiura, M., Watanabe, J., Akitsuki, Y., Sassa, Y., Sato, T., Matsue, Y., Kawashima, R., 2004. Mental visual synthesis is originated in the fronto-temporal network of the left hemisphere. Cereb. Cortex 14, 1376–1383.

Watanabe, T., 1998. A study on the individual differences of the experience of hypnagogic imagery. Shinrigaku Kenkyu: Jpn. J. Psychol. 68, 478–483.

Waxman, S.G., 1980. Determinants of conduction velocity in myelinated nerve fibers. Muscle Nerve 3, 141–150.