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Regional homogeneity, resting-state functional connectivity and amplitude of low frequency fluctuation associated with creativity measured by divergent thinking in a sex-specific manner

Hikaru Takeuchi[a,*], Yasuyuki Taki[a,b,c], Rui Nouchi[d,e,f], Ryoichi Yokoyama[g], Yuka Kotozaki[h], Seishu Nakagawa[i,j], Atsushi Sekiguchi[b,i,k], Kunio Iizuka[l], Yuki Yamamoto[i], Sugiko Hanawa[i], Tsuyoshi Araki[f], Carlos Makoto Miyauchi[m], Takamitsu Shinada[i], Kohei Sakaki[i], Takayuki Nozawa[n], Shigeyuki Ikeda[n], Susumu Yokota[a], Magistro Daniele[o], Yuko Sassa[a], Ryuta Kawashima[a,f,i]

[a] Division of Developmental Cognitive Neuroscience, Institute of Development, Aging and Cancer, Tohoku University, Sendai, Japan
[b] Division of Medical Neuroimaging Analysis, Department of Community Medical Supports, Tohoku Medical Megabank Organization, Tohoku University, Sendai, Japan
[c] Department of Radiology and Nuclear Medicine, Institute of Development, Aging and Cancer, Tohoku University, Sendai, Japan
[d] Creative Interdisciplinary Research Division, Frontier Research Institute for Interdisciplinary Science, Tohoku University, Sendai, Japan
[e] Human and Social Response Research Division, International Research Institute of Disaster Science, Tohoku University, Sendai, Japan
[f] Smart Ageing International Research Center, Institute of Development, Aging and Cancer, Tohoku University, Sendai, Japan
[g] School of Medicine, Kobe University, Kobe, Japan
[h] Division of Clinical research, Medical-Industry Translational Research Center, Fukushima Medical University School of Medicine, Fukushima, Japan
[i] Department of Functional Brain Imaging, Institute of Development, Aging and Cancer, Tohoku University, Sendai, Japan
[j] Department of Psychiatry, Tohoku Pharmaceutical University, Sendai, Japan
[k] Department of Adult Mental Health, National Institute of Mental Health, National Center of Neurology and Psychiatry, Tokyo, Japan
[l] Department of Psychiatry, Tohoku University Graduate School of Medicine, Sendai, Japan
[m] Graduate School of Arts and Sciences, Department of General Systems Studies, The University of Tokyo, Tokyo, Japan
[n] Department of Ubiquitous Sensing, Institute of Development, Aging and Cancer, Tohoku University, Sendai, Japan
[o] School of Electronic, Electrical and Systems Engineering, Loughborough University, England, UK

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ABSTRACT

Brain connectivity is traditionally thought to be important for creativity. Here we investigated the associations of creativity measured by divergent thinking (CMDT) with resting-state functional magnetic imaging (fMRI) measures and their sex differences. We examined these relationships in the brains of 1277 healthy young adults. Whole-brain analyses revealed a significant interaction between verbal CMDT and sex on (a) regional homogeneity within an area from the left anterior temporal lobe (b) on the resting state functional connectivity (RSFC) between the mPFC and the left inferior frontal gyrus and (c) on fractional amplitude of low frequency fluctuations (fALFF) in several distinct areas, including the precuneus and middle cingulate gyrus, left middle temporal gyrus, right middle frontal gyrus, and cerebellum. These interactions were mediated by positive correlations in females and negative correlations in males. These findings suggest that greater CMDT in females is reflected by (a) regional coherence (regional homogeneity) of brain areas responsible for representing and combining concepts as well as (b) the efficient functional connection (RSFC) between the key areas for the default state of cognitive activity and speech production, and (c) greater spontaneous neural activity (fALFF) during the resting of brain areas involved in frontal lobe functions, default cognitive activities, and language functions. Furthermore, these findings suggest that the associations between creativity and resting state brain connectivity patterns are different between males and females.

* Corresponding author.
E-mail address: takehi@idac.tohoku.ac.jp (H. Takeuchi).

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1. Introduction

A common definition of creativity is the ability to produce work that is both novel and useful within a certain social context (Runco and Jaeger, 2012; Stein, 1953). The most common measure to evaluate creativity is divergent thinking (DT) ["information retrieval and the call for a number of varied responses to a certain item" (Guilford, 1967)]. Indeed, performance on DT tasks can predict real-life creative achievement (for the meta analysis, see Kim, 2008).

The importance of brain connectivity for creativity has been predicted theoretically and demonstrated experimentally. Greater brain connectivity has been suggested to be essential for creativity because of the theoretical importance of combining disparate information (Heilman et al., 2003). Greater creativity is associated with the microstructural properties of widespread white matter areas (Takeuchi et al., 2010b) and greater functional connectivity between different brain areas during creative tasks (for a review of recent research, see Szameitat et al., 2002).

Recent studies have also shown unique associations between creativity measured by divergent thinking (CMDT) and resting-state functional connectivity (RSFC) for different brain regions. We have suggested that cognitive processes ongoing during rest, such as imagination, daydreaming, fantasy, and attentiveness to one's own feelings as well as the neural bases underlying these cognitive activities are shown or considered to be important for creativity (for summary, see Takeuchi et al., 2012). Previous studies using large sample sizes showed that greater CMDT is associated with greater RSFC between the key nodes of the default mode network (DMN; the network that is active at rest) (Takeuchi et al., 2012) as well as between the medial prefrontal cortex (mPFC), one of the key nodes of the DMN, and the language-related area of the left middle temporal gyrus (Wei et al., 2013).

Recent advances in analysis of resting-state functional magnetic resonance imaging (rsfMRI) have made it possible to reveal new aspects of resting-state brain activity (Chao-Gan and Yu-Feng, 2010). One such advance is fractional amplitude of low frequency fluctuation (fALFF), which is thought to indicate the magnitude of neural activity during rest (Chao-Gan and Yu-Feng, 2010; Zang et al., 2007) and a direct index of the spontaneous signal fluctuations underlying RSFC. Another measure is degree centrality (DC), which reflects the number of instantaneous functional connections between a region and the rest of the brain (Buckner et al., 2009). This measure is suggested to reflect how strongly a given region (node) acts as a cortical "hub" (Buckner et al., 2009), and thus, to reflect how strongly the node influences other brain regions and integrates information from functionally segregated regions. The third measure is regional homogeneity. This evaluates "*the similarity of time series of a given voxel to those of its nearest voxels in a voxel-wise way based on the assumption that a voxel was temporally similar to those of its neighbors*" (Yao et al., 2009). Using this method, we can measure the temporal homogeneity of regional BOLD signals, which can reflect the temporal homogeneity of neural activity and thus local connectivity of synchronization. These measures have been used to reveal the neural correlates of basic higher-order cognitive abilities such as intelligence, working memory, and attention (Cole et al., 2012; Takeuchi et al., 2015a; Tian et al., 2012; Xu et al., 2014). Given the extent brain connectivity and information integration as well as cognitive processes during rest have been shown and suggested to be important for creativity, we predict associations between CMDT and these neural mechanisms.

Sex differences in creative cognition have garnered attention in the field of cognitive science. The robust sex differences of divergent thinking scores are not consistently observed (Baer and Kaufman, 2008); however, a study has reported that a stronger positive association between creativity and psychopathology is observed in men than in women (Martín-Brufau and Corbalán, 2016). A review has concluded that declarative memory-related regions were strongly activated in men during divergent thinking, whereas regions involved in the theory of mind and self-referential processing were more activated in women (Abraham et al., 2014). Taken together, these studies have suggested the existence of sex differences in the neurocognitive mechanisms of divergent thinking. In addition, a previous study showed sex differences in the structural connectivity correlates of CMDT (Ryman et al., 2014). Similarly, our recent large-scale study (Takeuchi et al., in press; the subjects of this previous study and in the present study are the same, except for 59 subjects whose rsfMRI scans were unavailable) demonstrated a positive association between the CMDT and regional white matter volume (rWMV) across widespread white matter areas, including the temporal lobe, in females only.

Despite the attention CMDT has received in neuroimaging studies, no study has investigated DC/fALFF correlates of CMDT. A previous study has reported a negative association between CMDT and regional homogeneity in the precuneus (Chen et al., 2015). In addition, sex differences between DC, fALFF, regional homogeneity, RSFC, and correlates of CMDT have not been investigated. The purpose of this study was to investigate these issues.

As has been partly described, RSFC involving areas of the DMN and middle temporal gyrus were associated with verbal CMDT in a large sample (Takeuchi et al., 2012; Wei et al., 2013). Furthermore, the key nodes of the DMN, such as the precuneus and mPFC, are thought to be important hubs. Thus, we hypothesized that the DC, and regional homogeneity of these areas are associated with CMDT. Given the aforementioned (a) sex differences in the psychological correlates of CMDT (Martín-Brufau and Corbalán, 2016), (b) sex differences in brain areas that are recruited during CMDT (Abraham et al., 2014), and (c) recent reports on the existence of female-specific associations of CMDT and brain structural connectivity (Ryman et al., 2014; Takeuchi et al., in press), we expected to observe sex-specific (particularly female-specific) associations between connectivity measures and CMDT. Given the significant associations between CMDT and RSFC with the mPFC, a key node of the DMN (Takeuchi et al., 2012), we focused on the mPFC as a seed region for our RSFC analyses. We additionally investigated the associations of CMDT and fALFF, a direct index of the spontaneous signal fluctuations underlying RSFC as well as their sex differences to reveal the nature of the associations between resting state brain connectivity measures and CMDT.

Methods

Subjects

The present study, which is a part of an ongoing project to investigate the association among brain imaging, cognitive function, and aging, included 1277 healthy, right-handed individuals (732 men and 545 women). The mean age of the subjects was 20.8 years [standard deviation (SD): 1.8; range: 18–27 years]. All subjects were college, university, postgraduate, or graduate students from the previous year. All had normal vision and no history of neurological or psychiatric illness. Handedness was evaluated using the Edinburgh Handedness Inventory (Oldfield, 1971). Subject characteristics, recruitment, and exclusion criteria are provided in the Supplemental methods. Written informed consent was obtained from each subject for their participation in this project. All study procedures were approved by the Ethics Committee of Tohoku University.

Subjects were instructed to get sufficient sleep, maintain their conditions, eat sufficient breakfast, and to consume their normal amounts of caffeinated foods and drinks in the day of cognitive tests and MRI scans. In addition, subjects were instructed to avoid alcohol the night before the assessment.

The sex ratio in this study sample was unbalanced because the main participant pool was also unbalanced as females were less available.