ELSEVIER

Regional brain cerebral glucose metabolism and temperament: A positron emission tomography study

Yuko Hakamata [a], Mikio Iwase [b], Hiroshi Iwata [b], Toshiki Kobayashi [b],
Tsuneo Tamaki [b], Masami Nishio [b], Katsuhiko Kawahara [b], Hiroshi Matsuda [c],
Norio Ozaki [d], Shuji Honjo [e], Toshiya Inada [d],*

[a] *Department of Psychology and Human Developmental Sciences, Nagoya University,
Graduate School of Education and Human Development, Nagoya, Japan*
[b] *Nagoya Kyoritsu Hospital and Nagoya PET Imaging Center, Nagoya, Japan*
[c] *Department of Nuclear Medicine, Saitama Medical School, Iruma, Japan*
[d] *Department of Psychiatry and Psychobiology, Nagoya University, Graduate School of Medicine, Nagoya, Japan*
[e] *Department of Child Psychiatry, Nagoya University, Center for Developmental Clinical Psychology and Psychiatry, Nagoya, Japan*

Abstract

Personality, and in particular temperament, is thought to have a biological basis. In the present study, the relationships between regional brain glucose metabolism and temperament have been investigated. Regional brain glucose metabolism was measured using [^{18}F] fluorodeoxyglucose positron emission tomography in 31 healthy subjects. Temperament was assessed using the Temperament and Character Inventory. Temperament dimensions were observed to be significantly correlated with specific brain regions. In particular, novelty seeking was significantly correlated with the superior temporal gyrus, inferior parietal lobule, and the precuneus, which have been reported to be related with impulsiveness, while reward dependence was significantly correlated with the caudate head, which has been shown to be associated with reward processing. The various aspects of temperament may have biological bases in the specific brain regions. The accumulation of results from studies of this kind should provide further evidence connecting personality traits with their biological bases.
© 2005 Elsevier Ireland Ltd. All rights reserved.

Keywords: Positron emission tomography (PET); Fluorodeoxyglucose; Temperament and Character Inventory (TCI); Temperament; Personality

The development of functional imaging techniques in recent years has made it possible to explore some of the biological bases of personality. There has been a consequent increase in the number of studies investigating the relationships between brain activities, measured using functional imaging techniques, and particular personality traits, assessed using a specific personality model.

In these studies, Cloninger's personality model [4] that takes account of the theoretical biological bases of personality is frequently used. Cloninger's model describes personality as consisting of seven dimensions including temperament and char-

acter, and emphasizes that the formation of temperament can be involved in the activities of specific neurotransmitters. Temperament has four dimensions: novelty seeking (NS), harm avoidance (HA), reward dependence (RD), and persistence (PT). Although it has been reported that the different aspects of temperament may be modified depending on various states such as age (only NS) [2,3] and in the state of mood and anxiety disorders (mainly HA) [1,12], they are assumed to be genetically independent from one another, moderately heritable, and generally stable across time. NS is thought to be associated with dopaminergic activity, HA with serotonergic activity, and RD with noradrenergic activity. PT is not presumed to be related to a specific neurotransmitter because PT is the component derived from RD afterwards.

In many of the recent biological studies, a significant association between the different dimensions of temperament and brain activity has been reported using Cloninger's model. Recently,

---
* Corresponding author at: Department of Psychiatry, Teikyo University, School of Medicine, Ichihara Hospital, Anesaki 3426-3, Ichihara-shi, Chiba 299-0111, Japan. Tel.: +81 436 62 1211x2902; fax: +81 436 62 1511.
E-mail address: inada@med.teikyo-u.ac.jp (T. Inada).

Youn et al. [22] investigated the relationships between temperament dimensions and regional brain glucose metabolism in a [18F] fluorodeoxyglucose (FDG) positron emission tomography (PET) study and reported that NS was correlated mainly with the substantia nigra and several temporal regions, and HA and RD were correlated mainly with the temporal lobe and orbitofrontal gyrus. Since the substantia nigra and the temporal regions, which have been reported to be related to NS, are closely involved with dopaminergic activity, their results can be considered to support Cloninger's theoretical assumption. Furthermore, in other PET studies carried out using specific ligands, a significant association was found between the temperament dimensions and specific parameters such as dopamine D2 receptor density [20] and serotonin 2A receptor density [16]. However, there are several studies showing no association between the temperament dimensions and the specific parameters such as serotonin 1A receptor density [17] and dopamine synthesis capacity [13].

The precise relationships between different personality traits and related specific brain regions are controversial and remain to be clarified. In the [18F] FDG PET study presented here, the relationships between brain activity at rest and Cloninger's temperament dimensions were investigated in the Japanese population using a larger cohort than that used by Youn et al. [22].

This study was conducted after gaining approval from the Ethics Committee of the Nagoya PET Imaging Center. Written informed consent to participate was obtained from all subjects. Subjects were recruited from a healthy cohort who attended a medical examination at Nagoya PET Imaging Center. Those who suffered from Axis I psychiatric disorders or Axis II personality disorders of DSM-IV, as defined by the SCID-IV (First et al. [7]), or neurological or significant medical illness were excluded from the present study. To measure temperament dimensions, subjects were asked to complete a 60-item questionnaire on the four temperament dimensions (i.e., NS, HA, RD, and PT) extracted from the Japanese version of the Temperament and Character Inventory (TCI) (Kijima et al. [14]).

Subjects were scanned using an ADVANCE scanner (GE Medical, Ltd., USA), which has an intrinsic resolution of 4.8 mm full width at half maximum (FWHM) and simultaneously imaged 35 contiguous transverse planes with a thickness of 4.25 mm for a longitudinal field view of 14.8 cm. Before injection of the tracer, a 10-mm transmission scan was performed using triple GE-68 rod sources to correct attenuation. Emission scanning started after an intravenous injection of 200 MBq of [18F] FDG and continued for 7 min. All [18F] FDG PET scans were performed in a dimly lit room with no photic or auditory stimulation. During both the injection and PET scanning, subjects were asked to lie in the supine position with their eyes closed. At the beginning of the PET scanning, subjects were instructed not to engage in any activities. Gathered data were reconstructed in a $128 \times 128 \times 35$ matrix with a pixel size of $2 \, mm \times 2 \, mm \times 4.25 \, mm$ and were set at Subset 28, Itretion 5, using the ordered subsets expectation maximization (OSEM). Segmented attenuation correction was used with 3 mm of Gaussian filter for smoothing.

Spatial pre-processing and statistical analysis were performed using Statistical Parametric Mapping (SPM) 99

(Institute of Neurology, University College of London, UK) implemented in Matlab (Mathworks Inc., USA; Friston et al. [9,10]). All reconstructed images were spatially normalized into the Montreal Neurological Institute (MNI, McGill University, CA, USA) standard template to remove any intersubject anatomical variability [9,21]. The voxel size of normalized images was set at $2 \, mm \times 2 \, mm \times 2 \, mm$ matrix. The MNI co-ordinates obtained from the results of SPM 99 were converted into the Talairach co-ordinates using software that was downloaded from the following URL web site: http://www.mrc-cbu.cam.ac.uk/Imaging/Common/mnispace.shtml. Affine transformation was performed to determine 12 optimal parameters to register the brain on our original FDG template. Subtle differences between the transformed image and the template were removed by a nonlinear registration method using the weighted sum of the predefined smooth basis functions used in discrete cosine transformation. Spatially normalized images were smoothed by convolution with an isotropic Gaussian kernel with 12 mm FWHM. The effects of global metabolism were removed by normalizing the count of each voxel to the total count of the brain (proportional scaling in SPM). After the appropriate design matrix was specified, the condition of each voxel in each subject was assessed according to the theory of Gaussian fields. The exact level of significance of difference between conditions was characterized by peak amplitude. We focused on a cluster level to detect significantly different regions in the current study because our sample size was no so large for random field theory and so would lead to type II errors (pseudonegative). Fortunately, we had a certain amount of evidence for the relationship between personal traits and regional cerebral metabolism [22]. Therefore, we performed a priori study. To reveal the regions that were significantly correlated with each dimension of the TCI, multiple correlation analysis was performed for each voxel on the general linear approach between the personality dimension scores and the glucose metabolism. The NS, HA, RD, and PT scores were incorporated as covariates of interest. The resulting SPM $\{t\}$ value was converted to an SPM $\{z\}$ value for each personality dimension. The height threshold (u) used to interpret the correlation in terms of probability level was set at $z = 2.58$ ($P < 0.005$), with each cluster requiring a peak voxel of $z \geq 2.58$ without correction for multiple comparison. The extent threshold (k) was set at 100 voxels, this being sufficient to remove any small noisy clusters that may reach significance by chance.

A total of 31 subjects, 21 males and 10 females, were approved to participate in this study. Their mean age was 54 years (range: 38–73 years) and 50 years (range: 34–70 years), respectively. The mean TCI scores of NS, HA, RD, and PT in the present subjects were 49 (range: 33–62), 53 (range: 34–70), 41 (range: 20–53), and 14 (range: 10–18), respectively. Areas where the temperament dimension scores were correlated significantly with glucose metabolism are given in Table 1 and Fig. 1.

The NS score was positively correlated with the left superior temporal gyrus [Brodmann's area (BA) 13] and negatively correlated with the left inferior parietal lobule (BA7) and right precuneus (BA7; $P < 0.005$). The HA score was positively correlated with the right medial dorsal nucleus (thalamus) and