BRAIN and NERVE 69 (4): 375-381, 2017 Topics

The Roles of Brodmann Area 12: Gustation, Social Cognition, and Mental Time

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Abstract

Brodmann areas 11 and 12 are located in the orbitofrontal area. A voxel-based morphometric (VBM) study revealed a link between bilateral Brodmann areas 12/47 and taste disturbance in individuals with frontotemporal lobar degeneration (FTLD). In our VBM study of patients with Parkinson's disease, decision-making impairments were associated with atrophy bilaterally of Brodmann area 12, suggesting that this area may play an important role in social cognitive function. Our study also demonstrated that it may be involved in judgment of mental time.

Key words: Brodmann area 12; orbitofrontal cortex; taste; social cognition; mental time; voxelbased morphometry

Introduction

The following paper is based on a Japanese language version (BRAIN and NERVE, April 2017) by MK.

I start this review with Korbinian Brodmann's (1868-1918) own description of area 11 in his 1909 monograph[1]. Here he suggests that it may need structural sub-division

> Feld II — Area praefrontalis — bildet den oroventralen Teil des Stirnlappens an der Orbital- und Medianfläche, umfaßt also im großen ganzen den Gyrus rectus, den Gyrus rostralis und das vorderste Ende des G. frontalis Superior. Die Grenzen sind: medial der Sulcus rostralis superior, lateral ungefähr der Sulcus frontoniarginalis Wernicke und an der Orbitalfläche der Sulcus orbitalis internus.
>
> Gewisse feinere tektonische Unterschiede ließen sich innerhalb dieses Feldes noch machen und mit etwas Willkür auch räumlich abgrenzen. So könnte man das Gebiet zwischen dem S. rostralis sup. und dem S. rostr. inf. als besondere 3 reo rostralis von Feld 11 abtrennen; ebenso zeigen derGprus rectus und der medial davon gelegene Gpr. orbit. med. wieder gewisse Strukturdifferenzen, welche prinzipiell eine Scheidung gestatten würden (als Area recta und Area orbitalis interna). Ich habe aus Gründen der Übersichtlichkeit und da die Area histologisch ein geschlossenes Gebiet darstellt, in der Hirnkarte vorläufig nur ein Feld eingezeichnet, das sich ziemlich genau mit der Area praefrontalis von E. Smith deckt.
>
> [https://archive.org/stream/b28062449/b28062449_djvu.txt]
>
> Area 11—the prefrontal area—forms the rostroventral part of the frontal lobe on its orbital and medial surfaces, thus including most of the straight gyrus, the rostral gyrus and the extreme anterior end of the superior frontal gyrus. The borders are: medially the superior rostral sulcus, laterally approximately the frontomarginal sulcus of Wernicke, and on the orbital surface the medial orbital sulcus.
>
> It is possible to detect fine architectonic differences within this area and with some arbitrariness it can be subdivided. Thus one could separate the zone between the superior

rostral sulcus and the inferior rostral sulcus from area 11 as a specific rostral area; equally the straight gyrus and the medial orbital gyrus that lies medial to it demonstrate certain structural differences, which in principle permit a division (into an area recta and a medial orbital area).

For reasons of clarity and because this whole area forms a histologically circumscribed zone, I have tentatively only included one area in the brain map, coinciding fairly precisely with the prefrontal area of Elliot Smith. (Underlined by the author)

[translated by Laurence J. Garey, 1994
https://www.appliedneuroscience.com/PDFs/Brodmann.pdf]

Thus Brodmann's area 11 of 1909 could be subdivided. Furthermore, I show elsewhere in this special issue[2] that Brodmann in another brain map of 1910[3] places area 12 where he placed area 11 in 1909[1,4].

Kobayashi et al. [5] describe the process of delineating neuro-structural boundaries as follows:

The primary sensory cortex and motor cortex clearly differ from adjacent areas in layer structure with well-defined boundaries. However, layer structure changes gradually in the boundaries of some association areas. In such cases, even though typical parts of the adjoining areas are obviously different from each other, boundaries cannot be delineated clearly. Previous researchers – including Vogt, Campbell, Brodmann, and von Economo – also commented on this point, but their brain maps show clear boundaries for the sake of clarity. Following von Economo, von Bonin et al. classified cortical areas in macaque, chimpanzee and human utilize color gradation to indicate imprecise boundaries. (Underlined by the author)

This is the case with many brain regions and is why Brodmann had difficulty classifying cortical areas.

I. Location of area 12 and neuroanatomical tracts

Fig. 1 shows the location of human area 12, and Fig. 2 compares two of Brodmann's maps of the medial cerebral surface: one compiled in 1909[1] and the other in 1910[3]. In the 1910 map he placed area 12 within area 11 of the previous version. Areas 11 and 12 are both in orbitofrontal cortex. In frontal lobe, the lateral and orbital regions receive parvocellular and magnocellular input, respectively, in the dorsal medial nucleus of the thalamus.

As stated above, Brodmann did not include area 12 in human brain in his 1909 monograph. However, he was explicit about the existence of area 12 in the brains of guenon (Fig. 3), marmoset (Fig. 4), kinkajou (figure 105 of reference 1, p 183) and rabbit.

While Brodmann's research was intended to classify human brain areas, it should not be forgotten that he included studies of the animals listed below. In my opinion, cross-species studies thus formed an indispensable part of his research. Furthermore, this homological approach is essential to understanding human brain.

Areas 11 and 12 are said to be closely associated with the amygdala, hippocampus, hypothalamus, and striatum[6].

II. Functions of area 12

In 2011 we discussed area 12 in a paper[5] with the subtitle "An historical puzzle relevant to FTLD (frontotemporal lobar degeneration)". Thereafter we looked at patients with this disease and revealed that the orbitofrontal cortex centered on area 12 is associated not only with social, but also with temporal, cognition.

1. Gustation and olfaction

The posterior part of orbitofrontal cortex receives gustatory, olfactory, and visceral inputs while the anterior part receives visual, auditory, and somatosensory sensations. And in the anterior part the incoming information converges with taste and smell information. Whitwell et al.[7] conducted a voxel-based morphometric (VBM) study on cases of pathological sweet tooth (an obsessive liking for sweet food) among abnormal eating behaviors in patients with frontotemporal lobar degeneration (FTLD) and demonstrated a link with areas 12 and 47.

2. Social cognition

In patients with Parkinson's disease (PD), behavioral activities such as pathological gambling are observed more frequently than in normal individuals. The present author and others looked at this activity using a gambling task[8,9]. We then performed VBM analysis of structural brain abnormalities responsible for this behavior.[10]

Eighteen patients with PD and 37, elderly, healthy controls matched by age, sex, education and overall intelligence were tested on a computerized gambling task. Both patients and healthy participants underwent T1-weighted cranial MRI at 3 Tesla and Statistical Parametric Mapping 8 (SPM8) software was employed for the following: 1) *T*-test-based detection of areas reduced in volume in the PD group as compared to the healthy group, and 2) analysis of areas correlated with gambling task performance using the multiple regression module. The areas significantly correlated with gambling task performance and also identified with intracranial volume as covariate.

Behavioral analysis confirmed that the PD group behaved disadvantageously on the gambling task as compared to the healthy group. VBM findings included the following: 1) volume reduction in regions such as medial orbitofrontal cortex and inferior temporal lobe (Fig. 5) and 2) a statistically significant correlation based on multiple regression analysis between volume of lateral orbitofrontal cortex and gambling task performance (Fig. 6).

Medial, orbitofrontal cortex, volume reduced in the PD group, has been associated with longterm assessment of gains and losses.[11] On the other hand, the lateral orbitofrontal cortex, where volume correlated with gambling task performance, has been associated with recognition of losses[12]. Decision-making difficulties in patients with PD may result jointly from hypofunction of these different orbitofrontal regions.

Area 12 is likely to be associated with social cognition activities such as decision-making. And the functional differences between areas 11 and 12 need further clarification.

3. Time perception

Recent research has made rapid progress in understanding time perception and the brain regions involved[13]. Perception of temporal order and age awareness are discussed, in particular, in the context of confabulatory syndrome. Of the different types of confabulation, spontaneous confabulation signifies a "confusion of reality" more strongly than provoked confabulation, and Schnider points to its strong association with orbitofrontal cortex bilaterally – mainly in areas 11 and 12 and in particular the posterior medial regions (Fig. 7)[14].

The author and colleagues[15-17] also treated three females with limbic encephalitis who experienced retrogression of subjective age. Their autobiographical memories were consistent with past experience, and the symptoms separable from disorientation, amnesia, or confabulation. All three believed they were younger than they actually were and recollected real episodes. At the same time they could not recall experieces after the retrogressive age. On presentation they were thus temporarily living in the "past." With treatment and upon learning their correct ages, they recovered autobiographical memories and returned to the "present." We named this syndrome as autobiographical age awareness disturbance (AAAD).

Human memory is roughly classified into long-term memory and short-term memory, and autobiographical memory belongs to episodic memory, a type of long-term memory. In my opinion, episodic memory can be seen as mental time travel in that it recapitulates spatial and temporal relationships between given events, thus allowing mental travel from the present to the past.

Episodic memory consists of information about what, where, and when. These informational elements are integrated in the hippocampus and stored in the cerebral neocortex in a freely retrievable manner. It is this ability to create and retrieve episodic memory accurately that allows humans to recognize the present as the present and the past as the past. Disruption of this mechanism may result in misrecognizing the past as the present as part of AAAD (Fig. 8).

It is not known how subject age and “when” information work together as part of episodic memory. When we recall the past, yesterday’s memories are retrieved instantaneously and memories from three days ago, for example, may be tracked by date or name of the day. However, we may trace memories from ten, twenty, or more years ago by recalling our age at the time of remembered events. Thus age may play an important role in long-term mental time travel.

Human age awareness can be seen as a mental time function indispensable to humans to “live in the present.”

Concluding remarks

Although Brodmann made a distinction between areas 11 and 12, their precise functions are unknown and merit future research.

Acknowledgement

Supported by a Grants-in-Aid for Scientific Research (also known as KAKENHI) for Innovative Areas (JP25119006; JP18H05525).

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[Legends]

Table. Maps of animal brains published in Brodmann's 1909 monograph[1]

Animal species	Area 12	Areas 13-16 (insular cortex)
Human		
Guenon (Cercopithecus)	X	
Marmoset (Hapale)	X	
Lemur (Lemuridae)		X
Flying fox (Pteropus edwardsi)	X	
Kinkajou (Cercoleptes caudivolvulus)	X	
Rabbit (Lepus cuniculus)	X	
Ground squirrel (Spermophilus citillus)		X
Hedgehog (Erinaceus europaeus)		X

This book contains nine maps, in which the brain is divided into numbered areas, for human and other animals. Area 12 is located in guenon, marmoset, flying fox, kinkajou, and rabbit. The maps for lemur, ground squirrel, and hedgehog do not show area 12 but are explicit about the existence of areas 13 to 16 (insular cortex).

Fig. 1. Location of Brodmann area 12 in human brain.

Fig. 2. Comparison of Brodmann's 1909 and 1910 maps of the medial cerebral surface The

1910 version shows area 12, while it is absent in the 1909 version.

Reproduced with modifications from Kawamura M, Miller M W, Ichikawa H, Ishihara K, Sugimoto A: Brodmann area 12: an historical puzzle relevant to FTLD. Neurology 76: 15961599, 2011.

Fig. 3. Map of guenon brain presented by Brodmann in 1909.

Area 12 is included.

Reproduced with modifications from Brodmann K: Vergleichende Lokalisationslehre der Großhirnrinde in ihren Prinzipien dargestellt auf Grund des Zellenbaues. Barth, Leipzig, 1909.

Fig. 4. Map of marmoset brain presented by Brodmann in 1909.

Area 12 is included.

Reproduced with modifications from Brodmann K: Vergleichende Lokalisationslehre der Großhirnrinde in ihren Prinzipien dargestellt auf Grund des Zellenbaues. Barth, Leipzig, 1909.

Fig. 5. Relationship between decision-making performance and brain volume in patients with Parkinson's disease (VBM-based comparison with normal individuals).

Volumetric reduction is seen in regions such as medial orbitofrontal cortex.

Reproduced with modifications from Kobayakawa M, Tsuruya N, Kawamura M: Decisionmaking performance in Parkinson's disease correlates with lateral orbitofrontal volume, J Neurol Sci 372: 232-238, 2017.

Fig. 6. Relationship between decision-making performance and brain volume in patients with Parkinson's disease (multiple regression analysis).

In patients with Parkinson's disease, gambling task score correlated with volume of lateral orbitofrontal cortex.

IGT: Iowa gambling task.

Reproduced with modifications from Kobayakawa M, Tsuruya N, Kawamura M: Decisionmaking performance in Parkinson's disease correlates with lateral orbitofrontal volume, J Neurol Sci 372: 232-238, 2017

Fig. 7. Brain regions strongly associated with spontaneous confabulation

Reproduced with modifications from Schnider A: The Confabulating Mind: how the brain creates reality, Oxford University Press, Oxford, 2008.

Fig. 8. Model for human long-term temporal cognition.

A: Normal. Maintenance of human long-term temporal cognition critically depends on correct functioning of the network involving medial temporal cortex and the orbitofrontal cortex: this recognizes the present as the present and the past as the past.

B: AAAD. Disruption of the brain network for temporal cognition results in misrecognizing the past as present.

AAAD: autobiographical age awareness disturbance.

Reproduced with modifications from Kuroda T, Futamura A, Sugimoto A, Midorikawa A, Honma M, et al: Autobiographical age awareness disturbance syndrome in autoimmune limbic encephalitis: two case reports, BMC Neurol 15: 238, 2015.