Behavioural Brain Research 288 (2015) 11–19

Contents lists available at ScienceDirect

Behavioural Brain Research

journal homepage: www.elsevier.com/locate/bbr

Research report

Hemispheric specialization in affective responses, cerebral dominance for language, and handedness
Lateralization of emotion, language, and dexterity

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HIGHLIGHTS

- Hemispheric specialization in affective response seems to be related to language processing and motor preference.
- Lateralization in allocortical limbic areas shows specificity for emotion valence.
- Left amygdala activation is preeminent depending on emotional salience.
- Lateralization in mood regulation is defined better in right-handed than in non right-handed persons.

ARTICLE INFO

Article history:
Received 26 February 2015
Received in revised form 31 March 2015
Accepted 4 April 2015
Available online 13 April 2015

Keywords:
Emotion
Lateralization
fMRI
Amygdala
Subgenual cingulate
Anterior insula

ABSTRACT

Hemispheric specialization in affective responses has received little attention in the literature. This is a fundamental variable to understand circuit dynamics of networks subserving emotion. In this study we put to test a modified "valence" hypothesis of emotion processing, considering that sadness and happiness are processed by each hemisphere in relation to dominance for language and handedness. Mood induction and language activation during functional magnetic resonance imaging (fMRI) were used in 20 right-handed and 20 nonright-handed subjects, focusing on interconnected regions known to play critical roles in affective responses: subgenual cingulate cortex, amygdala, and anterior insular cortex. We observed a consistent relationship between lateralization of affective processing, motor dexterity, and language in individuals with clear right-handedness. Sadness induces a greater activation of right-hemisphere cortical structures in right-handed, left-dominant individuals, which is not evident in nonright-handed subjects who show no consistent hemispheric dominance for language. In anterior insula, right-handed individuals displayed reciprocal activation of either hemisphere depending upon mood valence, whereas amygdala activation was predominantly left-sided regardless of mood valence. Nonright-handed individuals exhibited less consistent brain lateralization of affective processing regardless of language and motor dexterity lateralization. In contrast with traditional views on emotion processing lateralization, hemispheric specialization in affective responses is not a unitary process but is specific to the brain structure being activated.

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http://dx.doi.org/10.1016/j.bbr.2015.04.006
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1. Introduction

Lateralization of brain functions is ubiquitous in vertebrates [1,2] contradicting the long-held belief that only *Homo sapiens* display significant hemispheric asymmetry [3]. This view was probably based on the fact that structural and functional asymmetry in the brain was initially defined for language-related areas [3–5]. With the discovery that brain functions other than language display lateralization in different species, e.g. singing [6] and visual specialization [7] in different avian species, a series of theories eventually emerged in relation to hemispheric specialization of different functions, including emotion processing. Two main theories evolved in relation to lateralization of emotion processing in the human brain. The "right hemisphere" hypothesis postulates that the right hemisphere is the main responsible for the processing of emotion, regardless of its positive or negative nature [8]. The "valence" theory [9] proposes that lateralization depends on the type of emotion; in this view, happiness and other affiliative emotions are processed predominantly by the left hemisphere and sadness is processed by the right hemisphere. In the present study we put to test a modified "valence" hypothesis of emotion processing lateralization, considering dominance for language and handedness rather than the actual side of the brain, in subjects with evidence for varying degrees of brain lateralization (i.e., right- and nonright-handed); such hypothesis considers motor preference, language, and emotion processing part of a general hemispheric specialization phenomenon.

To test this hypothesis, we used paradigms of affective response and language activation during functional magnetic resonance imaging (fMRI) in right- and nonright-handed persons. Although we set out to explore whole-brain effects of induced sadness and happiness, we also focused on interconnected regions previously shown to play critical roles in emotion regulation, namely, subgenual cingulate cortex, amygdala, and anterior insular cortex. The circuit connecting subgenual cingulum and amygdala is involved in emotional processing and social abilities in healthy conditions [10–12] and in major depression [13] leading to the hypothesis that variation in amygdala-subgenual cingulate circuitry is the origin of emotional and social deficits characteristic of it [13,14]. The amygdala is also pivotal in circuits modulating anxiety and fear [15,16]. In turn, insular cortex has been posited to be critical in the regulation of visceral activity, which is linked to emotional behavior, and in psychosis [17]. Thus, we used those areas as hypothesis-driven regions of interest (ROIs) in the present study.

2. Materials and methods

2.1. Participants

All participants were assessed at the Cognitive Neurology Section and the Psychiatry Department at FLENI Hospital, Buenos Aires. A total of 20 right-handed subjects (11 females, age 25.9 ± 5.6 years) and 20 non-right handed subjects (12 females, age 29.2 ± 9.7 years) participated in this study. Subjects were volunteers who did not receive financial compensation. Participants had no lifetime DSM-IV-TR diagnoses, and no first-degree relatives with schizophrenia, bipolar disorder, or depression as per their report. Participants were free from medications and chronic medical disorders including diabetes, major neurological and cardiovascular disorders per their self-report. They provided written informed consent as approved by the local bioethics committee, and in accordance with the ethical standards set by the 1964 Declaration of Helsinki.

2.2. Affective response measures

Subjects were also assessed for depression symptom severity with the Hamilton Depression Rating Scale [18] and for anxiety symptom severity with the Hamilton Anxiety Rating Scale [19] prior to fMRI scanning.

2.3. fMRI stimuli

FACES: subjects participated in a standardized affective response procedure, described in greater detail elsewhere [20]. fMRI data were acquired for two different affective conditions (happiness and sadness). Briefly, preceding the experimental conditions, subjects were shown a single slide with instruction on the task. Participants were told in Spanish: "During this task, I would like you to try to become happy [or sad] helping yourself with the faces showing such emotion". Subjects viewed the stimuli at their own pace and moved on to the next face with the aid of a response device by pressing two buttons simultaneously with the 2nd and 3rd fingers of the right hand. The mean time the subject spent looking at each picture in each condition was registered as "time to induce emotion".

In a debriefing session immediately after scanning, they were asked to complete self-assessment manikins (SAM) [21] on both arousal and valence associated with sad and happy faces. The SAM is a non-verbal pictorial assessment technique which can directly measure valence and arousal associated with a person's affective reaction to a wide variety of stimuli. It is later scored in a 9 point scale. Higher values for valence (picture of a smiling manikin) indicate happy affective reactions for a specific set of stimulus, whereas lower scores indicate sad reactions to them. Paired samples t test was used to compare valence of emotion induction for sad and happy stimulus in each group.

2.3.1. Block design of the affective response paradigm

Experimental design consisted of 2 sessions, one for sad responses and one for happy responses. Each session consisted of 3 blocks of task condition (sad [happy] faces) alternated with 3 blocks of baseline (fixation cross) of 60 s each block.

LANGUAGE: we used a category fluency paradigm to ascertain activation of language areas in individual participants. Subjects were shown a certain category in the screen (e.g., countries, colors, body parts) and asked to mention as many items in the category as possible. The paradigm consisted of 7 blocks of 30 s category fluency task alternating with 7 blocks of 20 s rest, for a total duration of approximately 6 min.

2.4. fMRI data acquisition

MRI data were acquired on a 3 T GE HDx scanner with an 8 channel head coil. Change in blood-oxygenation–level-dependent (BOLD) T2* signal was measured using a gradient echo-planar imaging (EPI) sequence. Thirty contiguous slices were obtained in the AC-PC plane (TR: 2 s, TE: 30 ms, flip angle: 90°, FOV: 24 cm, 64 × 64 pixels per inch matrix, voxel size = 3.75 × 3.75 × 4). A structural MRI was acquired with the T1-weighted 3D fast SPGR-IR sequence (120 slices, 1.2-mm thick slices, TR = 6.604 ms, TE = 2.796 ms, flip angle 15°, FOV 24 cm, 256 × 256 matrix). FACES and LANGUAGE sessions each consisted of 175 volumes.

2.5. Statistical analysis

2.5.1. Analysis of demographic and behavioral data

Continuous variables in Table 1 were compared by means of independent samples t-test. For comparison of discrete variables, the Chi Square test was used. In all cases, tests applied were two tailed and significance was assumed at $\alpha < 0.05$. All statistical analysis was performed with the SPSS version 13.0 software (SPSS Inc.).

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