ANNALES
UNIVERSITATIS MARIAE CURIE-SKŁODOWSKA
LUBLIN—POLONIA
VOL. LVI, 56 SECTIO D 2001

Department of Psychiatry, Medical University of Lublin
Department of Interventional Radiology and Neuroradiology, Medical University of Lublin

KATARZYNA KUCHARSKA-PIETURA,
RADOSŁAW PIETURA, MAREK MASIAK

Neural correlates of emotions in psychiatric patients in the light of functional neuroimaging findings

The neural substrates of human emotions have received marked attention recently. Several laboratories have used functional brain imaging techniques (fMRI, PET, SPECT, MRS) to investigate the neural correlates of emotions in normal and in pathology.

The aim of the current study is to present the recent neuroimaging findings concerning functioning of the "emotional brain" in psychiatric disorders.

ANXIETY DISORDERS

The following disorders: panic disorder, agoraphobia, specific phobia, social phobia, obsessive compulsive disorder, posttraumatic stress disorder, acute stress disorder, generalised anxiety disorder have been brought together in one large overall group called anxiety disorders (according to DSM-IV) or neurotic, stress-related and somatoform disorders in ICD-10 Manual because of their historical association with the concept of neurosis.

So far, efforts have been concentrated mainly on the reinforcement of a substantial proportion of these disorders with psychological causation, although the aetiology of these disabling disorders still remains a mystery.

Further application of the functional neuroimaging techniques is needed not only to determine a neural pathways responsible for anxiety disorders but also to understand mechanisms responsible for treatment efficacy. The focus of the review is on the newest studies that have used functional imaging techniques with particular emphasis on emotional background of the anxiety disorders. Evidence for functional brain abnormality in the genesis of neuroses will be discussed below.

GENERALISED ANXIETY DISORDER (GAD)

GAD characterises excessive anxiety and worry, occurring for a period of at least 6 months, about

the number of events or activities. The intensity, duration, or frequency of the anxiety and worry is far out of proportion to the actual likelihood or impact of the feared event (1).

SYMPTOM PROVOCATION IN GAD PATIENTS

The crucial role of the hippocampus with its afferent and efferent connections was highlighted in the genesis of anxiety.

R e i m a n and co-workers (1989) reported involvement of temporal poles in inducing various forms of anxiety. They described significant blood flow increases in the regions both in the production of normal anticipatory anxiety, lactate-induced panic and panic disorder (12, 13).

G u r et al. (1987) argued that severe anxiety is related to marked decrease rather than increased cortical perfusion, and related states of anxiety seemed to be associated with opposite effects on cerebral blood flow (rCBF). However, for low anxiety subjects, they found linear increase in CBF with anxiety.

Thus, to conclude, anxiety influences cortical brain activity, with possible differential effects on cerebral blood flow, depending on the anxiety level (8).

PANIC DISORDER

The essential feature of panic disorder is the presence of recurrent, unexpected panic attacks followed by at least 1 month of persistent concern about having another panic attack, worry about possible implications or consequences of panic attacks (1). What is unusual and rewarding from the point of view of diagnosis and therapy are studies which allow us to see human brain activity at the time of panic attack.

SYMPTOM PROVOCATION IN PANICS

PET findings across studies of lactate-induced anxiety attack among patient with panic disorder showed significantly increased activity in the right parahippocampal gyrus rather than decreased activity in the left. Moreover, the marked blood flow the increased bilaterally in temporal regions, insular cortex, claustrum, or lateral putamen and also in the vicinity of the left anterior cerebral vermis (12, 13). Interestingly, the anomaly was found only in patients with panic disorder who were vulnerable to lactate-induced panic. So, the question whether the asymmetry reflects a principal abnormality or whether panic attacks produce the secondary effect in brain areas associated with control of autonomic functions still remains open.

OBSESSIVE-COMPULSIVE DISORDER

The characteristic features of obsessive-compulsive disorder are recurrent obsessions or compulsions that are severe enough to be time-consuming or cause marked distress or significant impairment. Obsessions are persistent ideas, thoughts, impulses, or images that are experienced as intrusive and inappropriate and cause marked anxiety and distress (1). The current literature emphasises the neurobiological dysfunction within caudate, thalamus, anterior cingulate, and orbitofrontal cortex

in OCD patients who underwent cognitive and emotional challenge. Several authors have called themes a neuroanatomic circuit 'hyperactive' in OCD (2, 11).

Emotional stimulation

Functional neuroimaging has been also used to identify the neural correlates of patients with checking and washing symptoms who underwent disgusting stimuli (11). Washers revealed higher tendency to experience disgust than normal controls or checkers. Phillips et al. (2000) highlighted the differential neural mechanisms involved in perceiving disgust among washers and checkers. Statistically significant differences in neural responses to washer-relevant pictures were found. The washers rated these stimuli as more disgusting, frightening , and anxiety-evoking than controls and checkers. In both patient group there was prominent activation in visual regions and the insula. Checkers, however, showed marked neural activity in right frontal regions, the left thalamus and left caudate nucleus (11).

SOCIAL PHOBIA

The essential feature of social phobia is a marked and persistent fear of social or performance situation in which embarrassment may occur. Exposure to the social or performance situation almost invariably provokes an immediate anxiety response (1).

Emotional stimulation

Schneider et al. (1999) reported subcortical and cortical regions involvement in the processing of negative affect during presentation of neutral facial expressions as well as negative odour (14). Surprisingly, aversive emotional stimuli led to brain activity decreases in the amygdala and hippocampus among healthy volunteers, whilst social phobics demonstrated increased activation in both regions. These results also highlight a crucial role of the amygdala in the processing of negative affect and emotional learning, presumably by linking emotional reactions to external stimuli (9).

Another fMRI study in social phobia based on similar stimuli revealed both the amygdala activation during presentation of neutral faces and when patients were exposed to potentially fearful stimuli (5). Interestingly, social phobics revealed significantly greater bilateral amygdala activation to the faces than healthy controls, whereas in both groups the amygdala activation induced by odour were significantly high and comparable between the groups.

SPECIFIC PHOBIA

Specific phobia is characterised by marked and persistent fear of clearly discernible, circumscribed objects and situations. Exposure to the phobic stimulus almost invariably provokes an immediate anxiety response. The individual experiences a marked, persistent, and excessive or unreasonable fear when in the presence of, or when anticipating an encounter with a specific object or situation (1).

SYMPTOM PROVOCATION IN SPECIFIC PHOBICS

Fredrikson et al. (1993,1995) elucidated the neural correlates of specific phobia fear in

symptomatic spider phobics and snake phobics exposed to visual phobogenic and neutral stimuli using positron emission tomography. Their results showed the changes in regional blood flow (rCBF) presumably as the result of defence reaction during panic when conscious and voluntary cognitive processing might be reduced. According to the authors, the functional neuroanatomy of this reaction included significant decrease relative rCBF in hippocampus, prefrontal, orbitofrontal, temporopolar, and posterior cingulate cortex (6, 7).

Emotional stimulation

Previous functional neuroimaging studies have highlighted the neural activity of the secondary visual cortex during negative emotional states, even when they are induced by means other than visual stimuli (15).

AFFECTIVE DISORDERS

Studying patients with affective disorders provides a potential means of addressing what brain regions are involved in emotional regulation and how emotion influences higher cognitive processes. Moreover, neuroimaging studies allow to establish which brain regions were dysfunctional during a depressive episode and also how function in these regions covaried with resolution of the depressed state. Bench and co-workers (1992) scanned a cohort of depressed patients in an "at rest" condition, during illness, and again on recovery and compared them to healthy controls matched for age and sex (3). In depressed state they found significant relative deactivations in both supramodal and paralimbic brain regions that involved the anterior cingulate cortex, the left dorsolateral prefrontal cortex, and the left angular gyrus. Interestingly, activity within these regions normalised implying state, rather than trait, abnormalities (4). These findings might suggest that the identified pattern of hypoactivity represents an anatomical system involved in emotional regulation or the identified brain regions contribute to systems that mediate cognition, whose function has been modulated by inputs from some other region more critical to affective regulation.

SCHIZOPHRENIA

Several studies have demonstrated impaired facial expression recognition in schizophrenia. Phillips and co-workers (1999) have compared the neural correlates of facial expression perception in paranoid and non-paranoid schizophrenics and the healthy controls using fMRI. In three 5-min experiments, subjects viewed alternating 30-s blocs of black-and-white facial expressions of fear, anger or disgust contrasted with expressions of mild happiness. After scanning, subjects categorised each expression. The authors provided the distinction between two schizophrenic patient subgroups. In the paranoid schizophrenics, major regions of activation are shown in the fusiform and lingual gyri in response to fearful stimuli, and in the insula in response to expressions of disgust. In the non-paranoid patients, increased activation was found in the inferior temporal gyrus in response to anger, the middle temporal gyrus in response to fear stimuli, and in amygdala, superior temporal gyrus, thalamus in response to expressions of disgust. Paranoids were more accurate in recognising facial affect, and demonstrated greater activation than non-paranoids to most stimuli (10).

CONCLUSIONS

1. Functional brain imaging techniques are a very promising research tool in the study of "emotional brain" in normal and in pathology.

2. Neuroimaging studies did support the notion that pathological and normal forms of anxiety might share common neural correlates involving the temporal poles.

3. Deactivation in both supramodal and paralimbic brain regions was found in depression.

4. Schizophrenic patients showed reduced neural responses in amygdala, visual cortical regions, insula, inferior frontal cortex, anterior cingulate compared to normals during perception of facial expressions, respectively: fear, disgust and anger.

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2001.03.21

SUMMARY

The question whether there exists "the emotional brain" still remains open. The greatest scientific challenge at the threshold of 2000 is to make "a map of brain emotions" with a detailed topography for each "basic emotion".

The investigations, with the use of the most advanced neuroimaging techniques: positron emission tomography(PET), functional magnetic resonance (fMRI) and SPECT (single photon emission computed tomography), aimed at obtaining more precise location data on the system regulating the effect in normal and in pathology. In recent years, with the use of neuroimaging techniques, an important role of posterior temporal cortex, orbital-frontal cortex, amygdaloid nucleus and insula in the regulation of emotional behaviour has been indicated. The present study is an attempt at:

1) systemizing the research experiments serving the investigation of emotions with the use of neuroimaging techniques,

2) systemizing the latest results of investigations aimed at either search of the "emotional brain", or neural correlates of emotions responsible for the regulation of emotional behaviour in anxiety and affective disorders as well as in schizophrenic disorders.

Neuronalne korelaty emocji u pacjentów psychiatrycznych w świetle osiągnięć neuroobrazowania

Pytanie, czy istnieje „mózg emocjonalny", wciąż należy do otwartych. Największym wyzwaniem naukowym u progu 2000 roku jest sporządzenie „mózgowej mapy emocji" z wyszczególnieniem topografii dla każdej „podstawowej emocji". Celem badań z użyciem najbardziej zaawansowanych technik neuroobrazowania: pozytronowej tomografii emisyjnej (PET), funkcjonalnego rezonansu magnetycznego (fMRI) i SPECT (ang. *single photon emission computed tomography*) jest uzyskanie bardziej precyzyjnych danych lokalizacyjnych o systemie zarządzającym afektem w normie i patologii. W ostatnich latach przy użyciu technik neuroobrazowania wskazano na istotną rolę tylnej kory skroniowej, kory oczodołowoczołowej, jądra migdałowatego i wyspy w regulacji zachowania emocjonalnego. Praca ta jest próbą: 1) systematyzacji eksperymentów badawczych służących badaniom nad emocjami przy użyciu aparatury neuroobrazującej, 2) najnowszych wyników badań ukierunkowanych na poszukiwanie „mózgu emocyjnego" bądź skoordynowanych układów połączeń nerwowych odpowiedzialnych za regulację zachowań emocjonalnych w zaburzeniach lękowych, afektywnych i zaburzeniach kręgu schizofrenicznego.