Insular cortex – review

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SUMMARY: Recently, there has been a rising interest in exploring the role of the insular cortex and its vast connections with other brain regions. New studies describe it as a multisensory node that constantly receives information from the periphery, processes it and then forwards it to the superior parts of the cortex. It has been shown that insula participates in a large number of various cognitive processes including integration of perception, gustation, regulation of food intake, social interactions, empathy, pain processing and even takes part in pathogenesis of some neuropsychiatric disorders including anxiety, obsessive compulsive disorder and schizophrenia. All these findings open up possibility for developing new and improved treatment methods, as well as for better understanding of complex brain networking mechanisms.

KEYWORDS: insula, insular cortex, integration, perception, interoception, emotions,

Not so long ago, insular cortex and its functions were only at the margins of scientific interest and little attention was given to the examination of its role in all the cognitive processes it may be a part of. However, things have changed and advances in science created the possibility to explore this secret lobe that was hiding in the depths of the Sylvian fissure all along.

Recent studies of insular cortex show its multimodal functions and portrait it as some kind of integrative center or, better, a multisensory node that receives information from the periphery, processes it and then forwards it to the superior parts of the cortex. With new studies that keep flooding in, it has become clear that insular cortex participates in integration of perception, interoceptive awareness, social interactions, expressing empathy towards others, gustation, regulation of food intake, cognition, pain processing and many more functions that should yet be thoroughly examined.

In this review, I will try to summarize some of the most interesting new findings involving the insular cortex which will help us understand how it is tightly woven into our neural network and how it participates in our everyday cognitive processes.

Neuroanatomy and functions

Insular cortex, that often forgotten lobe of the mammalian brain takes its place in the depths of the lateral sulci in each of the cerebral hemispheres. It is hidden from the surface of the brain by three opercula: frontal, parietal and temporal and is positioned between piriform, orbital, motor, sensory and auditory cortices of higher order[1]. Central insular sulcus morphologically divides the insula into two parts: anterior and posterior[2]. The insula is interconnected with anterior cingulate cortex, rostral and dorsolateral prefrontal cortex, regions of the parietal and temporal lobes, as well as entorhinal cortex, amygdala, hypothalamus and dorsal thalamus. Accordingly, it is involved in viscerosensory, visceromotor, somatosensory, and interoceptive functions [3,4](Fig. 1). This specific location and projections sent by insula to other parts of the brain show us once again a diversity of its functions in processing various inputs from the outside world as well as form the inside reflecting our inner state.

Considering insula's cytoarchitectural composition in the primates' brains, it can be divided into three cytoarchitectural subregions based on the granularity of neurons in the cortical layer IV [5] (Fig. 2). According to this distinctive discrimination the ventral and anterior part of insula is part of agranular neocortex, posterior and dorsal insula show significant granularity while the middle insula shows dysgranularity. Also, worth mentioning is that great apes and humans display a subdivision of the agranular insular cortex in the very part of the ventral anterior section. This subdivision of insular cortex is positioned right next to the orbital cortex and is therefore called frontoinsular cortex (FI). In the frontoinsular cortex we can find clusters of neurons called von Economo neurons (VENs)[6]. It is believed that von Economo neurons in frontoinsular cortex together with agranular insular cortex of the anterior and ventral insula are involved in social awareness while granular and dysgranular insular cortices are important for receiving input about body's inner homeostatic state, as well as the somatosensory input from the periphery. Anterior part of insular cortex is also a major site of processing emotional, motivational, cognitive and sensory stimuli, as well as gustation. The intermediate dysgranular part of insula is widely connected with all the other parts of the insula and is involved in motor, somatosensory and pain processing[7], while the posterior granular part of insula forms a representation of our body's state constantly receiving information about our autonomic functions. This input is then carried to the anterior part of insula which integrates interoceptive input with the cognitive information adding subjective feelings to the experienced sensation[8].

Taking to consideration all of the above, it is clear that insula has a lot to offer and serves as a relay center of our brain, connecting

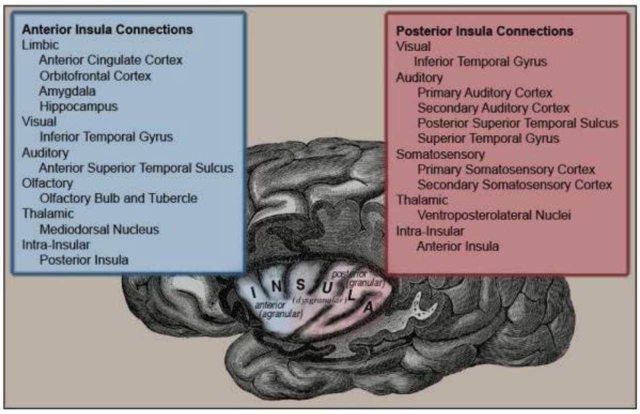

Fig 1. Subdivisions of the insula and their connections to other regions. The anterior insula, in blue, consists of the agranular and anterioventral dysgranular cytoarchitechtural portions of the insula and projects mostly to sensory and limbic parts of the brain. The posterior insula, in red, consists of the granular and dorsoposterior dysgranular cytoarchitechtural portions of the insula and connects to visual, auditory and somatosensory areas. Thalamic and intra-insular connections are observed in both areas. (Wylie & Tregellas, 2010)

and integrating information into one collective and undivided experience.

Insula and food related processes

Primary gustatory cortex consists of two substructures: the anterior insula on the insular lobe and the frontal operculum on the inferior frontal gyrus of the frontal lobe. That is a place where all the inputs from the oral cavity become integrated and cognitively processed. Our decision whether to take food or reject it depends not only on taste of the food, but also on its texture, temperature and odor. Neurons that are involved in our perception of taste, also receive somatosensory and olfactory projections from our oral cavity, as well as the input about body's energetic state from the periphery[9]. Projections from higher cortical centers make connections on those exact multimodal neurons and interfere with our perception of food and modulate the ways we feed.
The evidence that supports the theory about multisensory neuronal responses in the primary gustatory cortex was observed during electrophysiological recordings on monkeys[10]. In the experiment only one small group of neurons responded exclusively to taste stimuli (~6.5%) while ~23% of neurons responded during jaw or tongue movements. Recent studies seem to support these findings in humans as well. Maybe one of the best examples of somatosensory and gustatory integration of the received input is the fact that human anterior insular taste cortex becomes activated even by tasteless viscous stimuli (carboxymethylcellulose, CMC) 9. It has also been noted that water produces similar neuronal responses in the human taste cortex[11] which shows us an evolutionary aspect of eliciting responses in the taste cortex by substances important for modifying behavior and survival.

As mentioned earlier, the primary gustatory cortex doesn't just respond to basic stimuli which accompanies our experience of ingesting food (taste, texture, temperature, odor) but is also influenced by the input coming from higher-ordered brain structures involved in more advanced cognitive processes.
Simmons et al. [12] made an fMRI event-related experiment in which subjects were shown pictures of appetizing food and for comparison, pictures of locations. What they observed was that while both types of pictures activated the visual pathway, only pictures of food elicited the response in the gustatory cortex as well. Moreover, the image showing activated sites in the gustatory cortex was highly coincidental with the purely-taste elicited activity [13]. Besides appearance, motivational value and desirability of food ("food cravings") can elicit responses in human taste cortex just by imagining the properties of our favorite foods. Craving specific type of food increases activity in the brain rewarding pathways revealing intertwining connections between insular cortex and limbic structures[14].
Another fMRI human taste study done by Nitschke et al.[15] found that neuronal activity in our gustatory cortex can change dependent on our expectation of a tastant. They misled their subject into thinking that an aversive bitter taste would actually be less repugnant than it really was. After that, subjects reported the taste to be less aversive than when they had a truthful information about the nature of the taste. Brain imaging also showed reduced activity in the primary gustatory cortex.
Similar study referring on the modulation of our taste perception while expecting to detect taste[16] involved human subjects trying to detect taste in tasteless solution. The primary gustatory cortex was here also activated, proving that other cortical regions which are focused on finding and cognitively processing taste can also activate taste cortex even when there is no taste to be detected.

Input coming from visceral organs after food ingestion modulates neuronal activity in the taste cortex similar to one coming from an external stimuli or higher cognitive centers. These signals interfere with the cumulative data that is converging to the taste cortex and regulate our future food intake. This association between somatosensory and postingestive stimuli forms "memory trace" in the taste cortex which is responsible for differentiation between noxious and harmless food.
Gutierrez et al. experimented on rats in order to study the nature of neophobia (decrease in the intake of a solution where a novel taste was presented). This effect gradually disappears and the consumption increases from the second encounter with the taste. If gastric malaise is induced after first intake, rat will be opposed to taking the solution again and will develop long-lasting aversion to the tastant. After blocking muscarinic but not NMDA receptors in the taste cortex rat expressed aversion regarding the novel taste even though it was not harmful and did not elicit malaise. These findings suggest muscarinic receptors are the key in attenuation neophobia and formation of memory trace in the taste cortex. Same behavioral patterns can be observed in humans. For instance, if we experience nausea after eating certain type of food, we will associate that food with feelings of illness and discomfort and begin to avoid it in the future. These responses are partially reversible and depend on the gustatory cortex plasticity.[17]

Information regarding body's energetic balance has impact on insular activity as well. Neuroimaging shows different patterns of cortical activities during experiencing feelings of hunger and, in contrast, satiety[18]. These studies provide evidence that in hu-

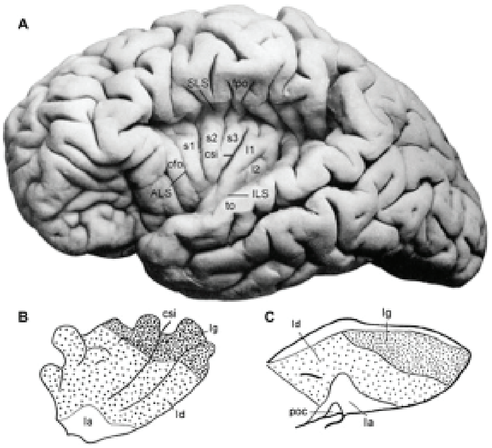

Fig 2. Lateral view of insular cortex. In (A) we see the left insula after the overlying opercula had been removed. (B) and (C) show cytoarchitecture of the insulae in Homo sapiens and Macaca mulatta. Both images display insular similar portions of granular (Ig), dysgranular (Id), and agranular (Ia) regions . The central sulcus of the insula (csi) is observed in humans. Other notations: Anterior limiting sulcus (ALS); first (s1), second (s2), and third short gyri (s3); first (l1) and second long gyri (l2); inferior limiting sulcus (ILS); orbitofrontal operculum (ofo); frontoparietal operculum (fpo); temporal operculum (to); piriform olfactory cortex (poc); superior limiting sulcus (SLS). (Bauernfeind et al., 2013)

mans, the insular cortex regions display stronger activation in cases of nutritional deficit whereas during satiety and overindulgence those regions are deprived. Another study showed negative correlation between level of insular cortex activity and insulin plasma concentrations[19], while other demonstrated that insular responses to pictures of foods decrease with satiety and increase again after intravenous administration of ghrelin, an orexigenic gut hormone[20].
Dispropotion in insular cortex activity can be seen between lean and obese subjects, in which the latter have increased resting insular activity [21] that leads to overindulgence in food and in the end – obesity. Such individual variation in representing body's internal state and regulating food-relating processes can represent one's susceptibility for gaining weight easily.

Insula, emotions and social awareness

New studies keep pointing out the role of insular cortex in emotional awareness. This means it is involved in processes of attributing emotional feelings to information coming from within our body[22]. Emotional awareness couldn't be achieved without interoception which is described as the sense of physiological condition of the body[23].

Many cortical regions, such as the anterior cingulate cortex, amygdala and ventromedial prefrontal cortex have been associated with interoceptive and emotional awareness, but insular cortex has been found to have the crucial role in these processes. Studies conducted on subjects who had focal epileptic seizures in anterior insular cortex reported heightened emotional awareness and feelings of wellbeing suggesting anterior insular cortex is the key part of insular cortex where this integration of input occurs [24]. Although anterior insular cortex has a dominant role in these processes, we should not forget that posterior insula recieves incoming data coming from all the tissues in the body and sends it over to anterior insula which adds a cognitive dimension to it. Gu et al. [25] suggested dual-process model in which anterior insular cortex has two major functions: 1) integration of bottom-up interoceptive prediction error signals with top-down predictions from higher-ordered cortical structures and 2) providing output of interoceptive predictions to visceral systems that serve as a point of reference for autonomic reflexes (Fig. 3). The integration of bottom-up and top-down signals is crucial to one's subjective awareness and consciousness [26]. We can say that anterior insular cortex acts as a correction switch correcting input coming from the viscera and sending it downwards again in order to re-adjust the settings of the previously flawed function.

Perceiving your own body state and being emotionally aware of processes occurring in order to maintain your inner balance is very important from the aspect of social interactions as well. That is because we recognize the same subjective feeling states we once experienced in others. It is a basis in applying empathy towards others and building strong intersocial connections inside a group 5. Social awareness end empathy are just two of many cognitive processes that take their place in the anterior insular cortex and are observed to be correlated with the presence of clusters of von Economo neurons in frontoinsular cortex and the size of insular cortex compaired to the brain size.
Bauernfeind et al. made a study in which they examined the relative size of insula and components of its cytoarchitectural subdivisions in humans and other primates to support the idea of evolved insular cortex in species with highly organized social structures. Point of interest was the presence of large spindle-shaped projection neurons with a single basal dendrite (von Economo neurons) that form a subdivision of agranular insular cortex (frontoinsular cortex) and are observed only in great apes and humans 6. In addition to the theory that connects von Economo neurons (VENs) and social awareness, it is notable that a severe loss of VENs and degeneration of this region are observed in patients with the behavioral variant of fronto-temporal dementia, a state in which an individual can not recognize the effect of his or hers actions on other's emotions. It has also been noted that the predominant activation of left or right insula depends on the types of emotions that an individual is currently experiencing. Therefore, the predominant activation of the right insula is associated with negative feelings and sympathetic function while the predominant activation of the left insula is associated with positive feelings and parasympathetic function[27].

In the previously mentioned study the main hypothesis was that the size of cortical area, in this case particulary the size of insular cortex, is directly proportional to the amount of information being processed in that region which is then observed as enhanced functional output. This improved functional output in species with highly evolved insular cortex may be of extreme importance for regions involved in processing social interactions.
Bauernfeind et al. observed positive allometric relationship between the insular cortex and total brain size, meaning that, as primate brain increases, the total insula volume tends to increase in size moderately faster than the rest of the brain. Insula in large-brained primates, great apes and humans, is also bigger than it is predicted by isometry and the anterior agranular insular cortex shows increase in its size at a greater rate than the dysgranular or granular insular cortices. Anterior portions of insular cortex

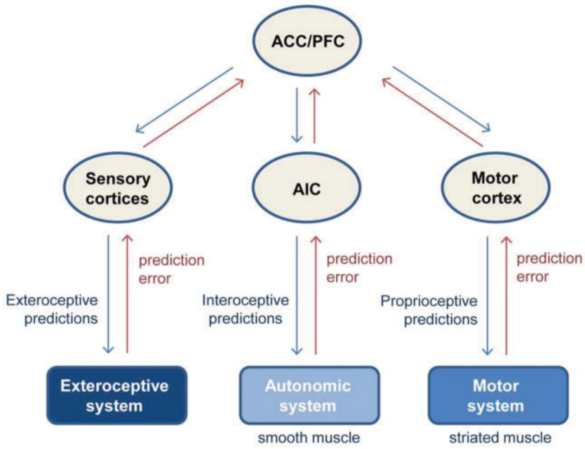

Fig 3. Proposed role of insula and emotional awareness. Similar to the role of sensory cortices in exteroceptive processing and motor cortices in proprioception, the anterior insular cortex integrates bottom-up prediction errors from lower-level structures with top-down interoceptive predictions from high-order brain regions such as the anterior cingulate cortex (ACC) and the prefrontal cortex (PFC). (Gu, Hof, Friston, & Fan, 2013)

show enlargement similar to one of the frontal cortex which is also disproportionally larger than the other non-frontal brain regions. In addition, the size of a social group has also showed an impact on the total insula size complementing the fact that living in complex social systems demands advanced information processing in insular regions underlying social awareness.[5]

Evolution of insular cortex as a result of complex social interactions enrich our lives with possibilities of showing empathy toward others, acknowledging other individual's mental states and acting in a cooperative manner.

Insula and pain perception

Insular cortex is very important in modulating afferent information and integrating it with cognitive mechanisms of higher order. This integration of incoming information constructs individual's subjective sensory experience. Being aware of and acknowledging differences in sensory input is of crucial importance in our everyday life. One of the most valuable sensory modalities designed to save us from harmful experiences is the perception of pain. Activation of insular cortex has also been correlated with the intensity of noxious stimulation and so it may be that this brain region possibly takes part in pain intensity coding[28].

If there is an impairment in processing afferent nociceptive information from the periphery, our perception of pain differs from one observed in healthy individuals and may lead to asymbolia, a condition where individuals can detect noxious stimuli as painful but can not tell the significance of such stimuli and because of that they show inadequate responses regarding pain [29].

Starr et al. conducted an experiment in order to describe the importance of insular cortex in pain processing. A focus of the study were two male patients with large left middle cerebral artery (MCA) strokes with lesions involving insular cortex and different parts of adjacent brain regions. In contrast, fourteen healthy subjects were studied as well.
They wanted to find out if there was a difference in pain perception between affected (right) side and unaffected (left) side of the body while applying heat in a various range of temperatures as a noxious stimuli. Although both patients exhibited some differences in their responses to noxious stimuli which is probably due to diversity of their lesioned brain areas (Fig. 4), they both experienced elevated pain ratings and sensitivity.
In control group, with each noxious stimulus the insular cortex showed bilateral activation, whereas the stimulation of affected (right) side of the body in patients with left insular lesions did not produce ipsilateral insular activity. These results suggest that contralateral insular activation seems to be necessary in order to produce ipsilateral insular activation.[30]

Both patients also exhibited greater responses in primary somatosensory cortex (SI) during stimulation of affected (right) side of the body when insular activation was not present. In absence of the insular function it is possible that other brain regions, in this case mostly the primary somatosensory cortex (SI), help in processing of nociceptive information that can not be properly handled without the insular contribution of signal transduction. Even though this information suggests insular cortex is not necessary for cognitive confirmation of pain, it is obvious that it has a major role in modulation of incoming nociceptive signals and tuning the activity of somatosensory cortical regions accordingly. It is also a possibility that insular lesions are responsible for loss of descending inhibitory projections since insular cortex is connected to regions like anterior cingulate cortex and dorsolateral prefrontal cortex 31 that activate the periaqueductal gray (PAG) within the tegmentum of the midbrain which is the primary control center for descending pain modulation.

Another possibility is that insular cortex has impact on various cortical regions involved in pain perception and is involved in tuning down the incoming pain signals via its multiple cortical-cortical interactions[30]. Some studies even suggest that top-down signals involved in pain modulation can be altered due to our internal knowledge regarding the nature of the stimuli. That way insular cortex and its projections can tune down cortical responses if they decide that the noxious stimulus is safe. Cognitive states that are directly linked to this information processing pathway are mood, previous experience, expectation and emotion. Obviously, when the insular function fails, that process can no longer be observed and in contrast results in elevated pain ratings[30].

Insula and neuropsychiatric disorders

Insular cortex is extensively connected with many cortical areas and limbic system so it is hard to say it has a paramount role in any of the various neuropsychiatric disorders that are thoroughly being studied these days.
Integration of external sensory input with the subjective cognitive input from higher-ordered cortical regions is the basis for experiencing the awareness of your own body's state. Many deficits that are observed in neuropsychiatric disorders, especially in cases of anxiety, obsessive compulsive disorder and schizophrenia,

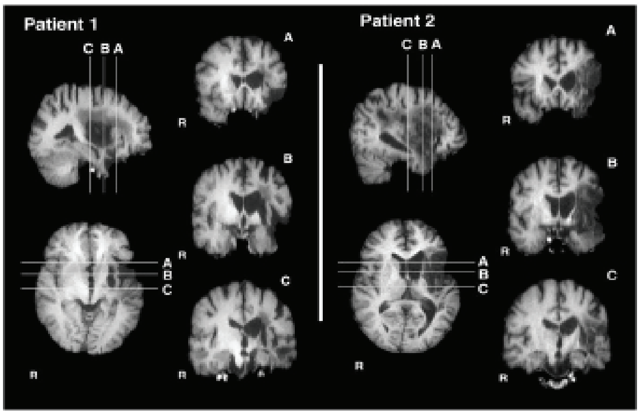

Fig 4. MR imaging pictures showing the extent of the lesions. Both patients had the severe left middle cerebral artery (MCA) strokes within the insular cortex. Patient 1's lesions involved large portions of the insula, parts of second somatosensory cortex (SII), basal ganglia, and white matter. Patient 2's lesions were more extensive than patient 1's and involved large portions of the insula and SII, parts of basal ganglia and white matter. Patient 2 also suffered from hemorrhagic transformation of the ischemic stroke.(Starr et al., 2009)

show a mismatch in these functions and could possibly relate to insular pathology.
Although findings and studies regarding insular role in these disorders have barely scratched the surface, there is some encouraging evidence suggesting that insular cortex has certain impact in their pathology.

Altered interoception could be one of the main reasons for experiencing elevated rates of anxiety and is seen in people who exhibit an inadequate interoceptive prediction signal. That means that they detect greater difference in observed and expected body states which ultimately leads to augmented rectifying top-down signals. These signals trigger an increase in anxiety, worrisome thoughts and other avoidance behaviors.[32]

One of the most debilitating anxiety disorders is surely the obsessive compulsive disorder (OCD). Due to amplified rectifying top-down signals, patients experience high rates of anxiety, worried thoughts and compulsive repetitive behaviors that are needed to attenuate the anxiety.[32]

Neuroimaging studies in unmedicated OCD patients with predominant checking symptoms showed morphometric differences in insular subregions where anterior insular cortex was enlarged and the posterior insular cortex reduced in volume. In contrast, healthy control group, as well as OCD patients with predominant cleaning symptoms, didn't show any morphometric alterations in volumes of insula's subregions.[33]

Differences in volume of insular subregions may be the result of disrupted neurodevelopment. Insular cortex is the first cortical region that develops in the human fetal brain and the anterior and posterior parts of insula differentiate from each other between 27 and 28 gestational weeks [34]. If something is to disrupt the course of this natural process, insular cortex will develop differently and that will have repercussions on total neuronal networking and brain functioning. When the posterior insular cortex is reduced in size, it can be expected that the anterior insular cortex will be larger in order to compensate for declined neural growth in the posterior portion. Greater number of neurons in the anterior insula are the reason for increased cortical activation in this region which in the end leads to exaggerated interoception as the main cause of obsessive behaviors seen in those patients.

Pathology of schizophrenia is also linked with insular malfunctioning, but the very nature, as well as the etiology of the disease still remains unknown.

One of first associations that comes up in mind while talking about schizophrenia is probably the inability of patients to discriminate between 'the self' and 'non self'. Considering the insular role in self-awareness and self-recognition it becomes clear why it is postulated that insula could have greater impact in development of the disease than it was previously thought. Patients with schizophrenia have difficulties recognizing pictures of their own faces from that of strangers and perceiving their own body[35]. Another problem arising from lacking sense of self awareness is the inability to differentiate between self-generated and externally-generated sources of sensory stimuli which could be the reason why some patients actively experience hallucinations[35].

Structural magnetic resonance imaging often shows decreased gray matter in the insular cortex which is usually observed bilaterally, but can also be absent. Bilateral decrease in insular gray matter shows positive correlation with the severity of hallucinations. These hallucinations are the result of faulty processing in the insular cortex involved in discrimination of visceral input from external input and attributing internal sensations to some external source.
Insula-related symptoms and functions that are often altered in patients with schizophrenia also include inability to recognize other people's emotions and facial expressions, inability to add an emotional dimension to any visual or auditory information and inability to express empathy toward others.[35]

Although many more research and studies need to be conducted in order for us to better understand the underlying causes of neuropsychiatric disorders and to improve methods used in treatment of these disorders, it is more and more obvious that insular cortex and its vast connections to other cortical regions play a key role in some of the leading symptoms that are the hallmarks of previously mentioned conditions.

Insula and 'phantom limbs'

Insular role in self-awareness can be affected in many conditions and not only in neuropsychiatric disorders. This so called self-evident status can easily become altered after brain damage involving the insular cortex.
This condition is called 'anosognosia' and is observed in patients who had recently suffered from a stroke and are unable to realize that their limbs are not functioning normally or they may even experience their own paretic limb as something that no longer belongs to them. Such patients often try to push

their paralyzed limb out of bed because they are convinced it belongs to some other person. State in which patients attribute ownership of their own limb to someone else is called 'somatoparaphrenia'.[36]

Mapping of 27 stroke patients with right brain damage showed overlapping results of serious cortical damage in the area of the posterior right insula which led to a conclusion that posterior insula is involved in experiencing our own contralateral body parts being involved in a movement and is crucial in processing of our self-awareness[36].

That is not surprising taking to consideration its multiple connections with somatosensory cortical areas and constantly receiving afferent information from the periphery. Some studies have presented evidence it is connected to motor areas as well [37].

The impairment in function of the right posterior insula is not commonly observed in hemiplegic/hemiparetic patients without anosognosia[36].

Supporting evidence, which explains the role of the posterior insula in acknowledging a movement of the limb as your own, comes from the experiment where healthy volunteers had to indicate whether movements they saw corresponded to their actual executed movements or were controlled by someone else. Subjects used a joystick to drive a circle along a T-shaped path. They were told that the circle would be driven either by themselves or by the experimenter. In this study, Farrer et al. observed decreased activity in the posterior insula when subjects stated the feeling that they did not control the movement. In that case, decreased activity is a result of the mismatch between what the subjects did and what they saw. On the other hand, the activity of the posterior insula was high when the visual input matched the afferent information coming from the limb that executed the movement.[38]

The present data suggest the right posterior insula, commonly damaged in patients with anosognosia, is of crucial importance for eliciting awareness of our own contralateral body parts and their movement. But we should always keep in mind the limitations of the conducted studies and scarce data which are still not providing enough evidence or answering why the right hemisphere is more commonly affected in patients with anosognosia. The answer could also lie, not only in deficits of the posterior insula, but also in the widespread and disconnected regions of the right hemisphere that might also contribute to the pathogenesis of the disease[36]. We can only hope that future studies will answer some of these questions.

Conclusion

Insular cortex is a versatile anatomical structure involved in many neural processes needed in our everyday lives. It processes sensory information coming from external stimuli as well as visceral information coming from within our body. It is involved in experiencing all modalities of taste, texture and odor of food we eat; participates in regulation of food intake and could be responsible for some types of obesity; processes tactile, thermal and nociceptive input arriving from the outside world; enables us to show empathy toward others and cooperate with them in large and complex social structures; provides us with the feelings of self-awareness and ability to differentiate 'the self' from 'nonself'. Not to mention its possible role in pathogenesis of various neuropsychiatric disorders including anxiety, obsessive compulsive disorder and schizophrenia.

All these findings are the basis for improving current treatment methods and to explore further the field of this often forgotten brain region. Acquiring new data, conducting large number of studies and raising interest in this subject could really help unveil the remaining mysteries of the insular cortex. Hopefully, new insights on this matter could help us better understand brain networking mechanisms, as well as their role in proper body functioning and conditions in which these mechanisms are compromised.

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Inzula- pregled

SAŽETAK: Nedavno se pojavilo veliko zanimanje vezano za ulogu inzule i njezine povezanosti sa ostalim regijama mozga. Nova istraživanja opisuju je kao mjesto gdje pristižu informacije sa periferije, zatim se ondje obrađuju i potom šalju dalje prema nadređenim dijelovima korteksa. Pokazano je kako inzula sudjeluje u velikom broju različitih kognitivnih procesa među kojima su: integracija percepcije, doživljaj okusa, regulacija hranjenja, društveni odnosi, empatija, doživljaj boli, kao i sudjelovanje u patogenezi nekih neuropsihijatrijskih bolesti poput anksioznosti, opsesivnog kompulzivnog poremećaja i shizofrenije. Sva ova dostignuća omogućuju nam razvoj novih i poboljšanih metoda liječenja, ali i bolje razumijevanje složenih neuralnih mehanizama.

KLJUČNE RIJEČI: inzula, inzularni režanj, integracija, percepcija, interocepcija, emocije