IDIAP COMMUNICATION

THE ANTERIOR CINGULATE CORTEX

Perruchoud Loïse [a]

IDIAP-COM -08-02

APRIL 2008

[a] IDIAP Research Institute

The Anterior Cingulate Cortex

Abstract

The anterior cingulate cortex is part of the human neocortex. Located dorsal to the corpus callosum, the ACC has many important functions: related to motivation, attention, pain perception and most importantly error detection, monitoring and evaluation. To perform these functions, the ACC needs to be connected directly or indirectly to most of the brain, especially the medial frontal, prefrontal and lateral prefrontal cortices. Some other connections are the basal ganglia, the limbic system and some part of the parietal cortex. To explain the different functions of the ACC, at least two theories have been developed: the conflict monitoring theory and the reinforcement learning theory which is the most inclusive theory up to now.

1. Introduction

The Anterior Cingulate Cortex (ACC) is an area of the brain situated on the medial surface of the frontal lobes (3). It forms the anterior part of the cingulate cortex located above and around the corpus callosum. It is divided into four parts: rostral (towards the front), caudal (towards the back), dorsal (at the top) and ventral (at the bottom). The ACC consists of spindle-shaped neurons that can only be observed in humans and to a lesser extent in great apes, which means that it is an evolutionary specialization of the neocortex. These neurons project to different areas of the brain including the basal ganglia, motor areas and the spinal cord. The functions of the ACC can be divided in two main categories which correspond reasonably well to the rostral and caudal parts stated above. The rostral ACC has an executive function that is important in error detection while the caudal ACC has an evaluative function that reduces competition between incompatible stimuli (3). The ACC is one of the most important areas when dealing with errors, error potentials and EEG studies because it is believed to be the source of these errors in terms of brain potentials.

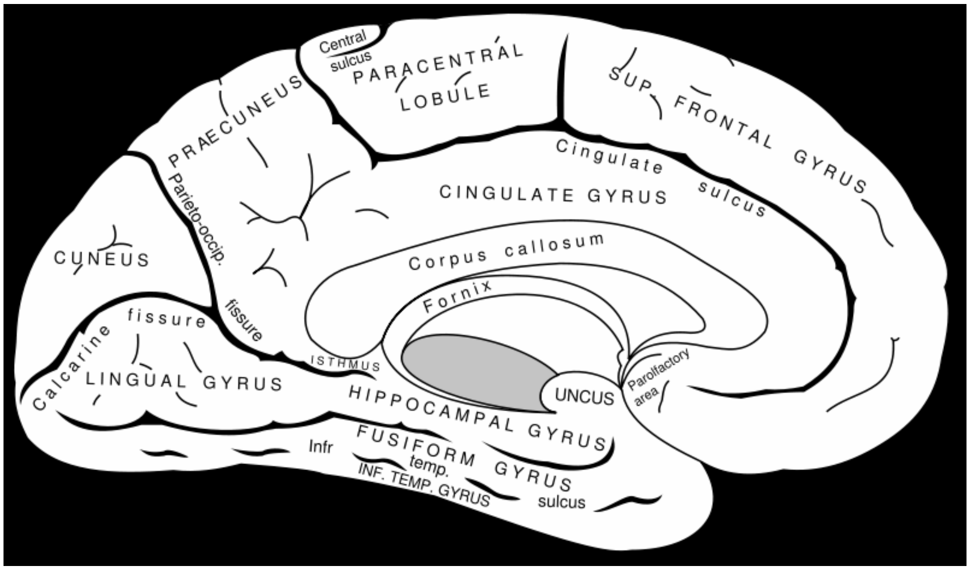

Figure 1 Medial surface of left cerebral hemisphere (14)

2. Functions of the ACC

The ACC along with the prefrontal cortex plays an essential role in attentional behaviours. It is active especially when there is an effort required. This area is also believed to be specialized in error detection and processing, response conflict, assignation of appropriate control to other areas in the brain, losses of reward and other negative events such as pain perception (4). In response monitoring, the ACC checks and compares the outcome of an event against the expected event. Therefore, if the intended action and the action itself are different, the ACC sends information to other neurons in order to modify the action and obtain what was intended. Other functions are anticipation of tasks, motivation and modulation of emotional responses (14).

Dopamine (a neurotransmitter linked among other things to many mental disorders) is also necessary to mention as a function of the ACC. The lower the dopamine level, the higher the activity of the anterior cingulate cortex (for more information see section 4.2). In addition the ACC is also tightly connected to the brainstem and spinal cord and therefore, regulates autonomic and motor activities such as respiration and blood pressure.

As mentioned in the introduction, the ACC can be relatively well divided in four parts: the dorsal, caudal, ventral and rostral part. The anterior ACC has an executive function while the ventral ACC is involved in emotions. The dorsal region is sometimes related to attention and to autonomic control but its main function is cognition. The caudal ACC focuses especially on cognition and evaluation of errors. In addition, the dorsal/caudal region has a role in cognition and higher-order motor processes. When making an experiment, the caudal ACC will be active when there is strong competition and the rostral ACC will be engaged when errors are made. Although I divide the anterior cingulate cortex in several parts, most of the functions are interconnected and connected to other regions in the brain (1).

3. Connections of the ACC

The anterior cingulate cortex belongs to the neocortex, which means that it appears almost exclusively in humans. This area contains special neurons called spindle-shaped neurons that are found only in humans, great apes and some whales. Therefore, the ACC is a specialization of the cortex that developed, because it gave an evolutionary advantage to the individuals who had it (1).

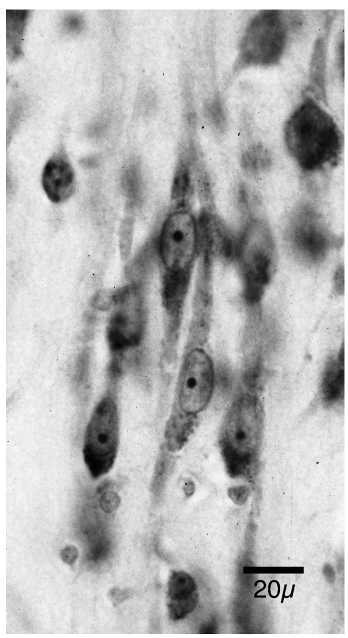

Figure 2 A pair of spindle cells in human anterior cingulate cortex

Because the ventral ACC is involved in emotional behaviours, it is part of the limbic system. Connections to other medial limbic areas, such as the hypothalamus, hippocampus and the amygdala among others are well-defined. In addition, these areas are also linked to motivational and affective behaviours (9). The ACC is also associated with brainstem structures (involved in autonomic control) since one of the functions of the anterior cingulate cortex is to control autonomic behaviours like heart rate and blood pressure (1). The lateral frontal and parietal areas have connections with the ACC as well.

The major areas that are tightly associated with the ACC in error processing are the basal ganglia, the medial frontal and prefrontal cortices (PFC). The basal ganglia seem to be connected to the ACC because of its role in actions correction. The medial frontal cortex helps the ACC in monitoring and maintaining ongoing behaviour. "The prefrontal cortex detects incompatible response options on incongruent trials and signals conflict-resolution processes" (12). Theses conflict-resolution processes are probably done in association with the presupplementary motor area situated in the vicinity of the cingulate cortex. Additionally, the lateral PFC detects competing response options and resolves the conflict in communicating with the dorsal ACC, the posterior cingulate cortex and the presupplementary motor areas (12). Therefore, the PFC, similar to the anterior cingulate cortex, has an action monitoring activity and is engaged in the decision making process. Besides, the lateral PFC also sends information about planning, sequencing of behavior, language, attention and working memory to the ACC (10).

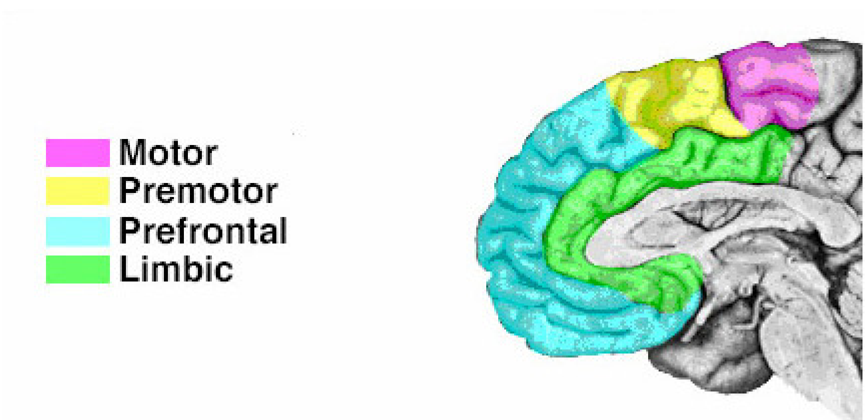

Figure 3 The prefrontal and the limbic system

Finally, scientists have discovered that some neurons of the ACC known as pyramidal neurons have long-distance connections directly or indirectly with most of the brain, but it is very difficult to find exactly where they go.

4. Lesions studies

The lesions studies are extremely important while studying human beings. The best way to understand the function of an area is to study what happens after the ablation of this region. However, because of obvious ethical problems, it is impossible to deliberately destroy the ACC of a person and look at the result. Therefore, scientists study patients that have a brain injury and ask them to participate in experiments to learn what goes wrong when the area is missing. Using this method, it has been discovered that people with reduced or no ACC activity experience akinetic mutism , diminished self-awareness and depression, motor neglect and impaired motor initiation, reduced responses to pain and aberrant social behaviours (5). Other problems associated with the lack of this area are inability to detect errors, severe difficulty with resolving stimulus conflict, emotional instability, inattention (14), apathy and dysregulation of autonomic functions (2). On the other hand, seizures in the ACC "impair consciousness, alter affective state and expression and influence skeletomotor and autonomic activity" (5). Psychopathic and sociopathic behaviours, tics, OCDs (obsessive-compulsive disorders) and other aberrant social behaviours have also been noticed in these patients.

Other mental disorders have symptoms related to ACC malfunction. Schizophrenic people, for example, are known for having difficulty in dealing with conflicting spatial locations in a stroop-like task and abnormal ERNs. ADHD (attention-deficit-hyperactivity disorder) patients have reduced activation in the dorsal area of the ACC and OCD patients seem to have low levels of the glutamate neurotransmitter (14).

5. Functional theories about the ACC

Many theories have been proposed to explain the function of the ACC in error processing. No theory, for the moment, can entirely explain all the experiments that were realized on the ACC because it is complicated to integrate the cognitive and the affective parts of this area. Nevertheless, there are essentially two sorts of evidence about the

ACC: the electrophysiological studies (coming from EEG studies) and the imaging studies (from fMRI studies).

In the years 2000, there were two theories trying to explain what goes on in the ACC: the conflict monitoring theory and the error detection theory (12). Today, the error detection theory has been abandoned due to the lack of integration of the affective part of the ACC (2). The error detection theory was based essentially on the fact that the ACC detected and monitored only errors and not correct responses which is actually the case. Many scientists found evidence showing that an ERN formed after a conflict. Because ERNs also appeared during high conflict stimuli, the error detection theory was discarded.

The conflict monitoring theory is still envisioned today but a new theory has risen that seems to encompass more data than any other theory. This theory known as reinforcement learning theory takes into account the results of feedback negativities.

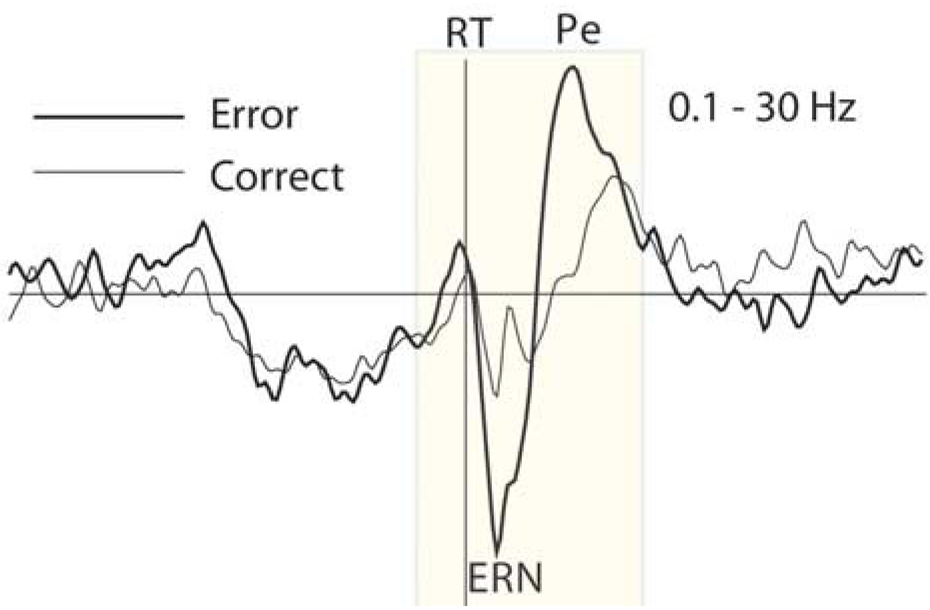

Figure 4 Error-related negativity waveform

In order to explain what this theory is about, the concept of ERN needs to be understood. An ERN or error-related negativity is a negative waveform produced by the brain and recorded by an EEG (electroencephalogram) after the occurrence of an error or a conflicting event. In this theory, errors are viewed as negative or undesirable events (13) that give feedback to subjects in order to adapt and adjust their behaviour. In other words, people can learn from their mistakes and the next time the same action is processed, it will occur faster and with more assurance than the first time.

The RL theory is based on feedback ERNs: The feedback of an error always follows the response. Therefore, the feedback ERN cannot be explained by the response conflict. This is what is different from other theories. The reinforcement learning theory poses that there is a difference between an event and its intent. At the time a difference occurs, the brain, especially the ACC, produces an ERN and sends information to the concerned areas to resolve the problem using dopamine neurons. (For more information, see section 4.2)

5.1. The imaging studies

The imaging techniques include PET and fMRI. They have helped a great deal for the study of the ACC functions, especially in defining the connections of both parts of the ACC (the affective and the cognitive) (2). These studies also showed that the main function of the ACC is the monitoring of conflicts which brings us to the first of the theories described above: the conflict monitoring theory or conflict theory (14). All these connections that were found with these studies are used by the ACC to handle a conflict whenever it is detected in delegating the tasks to be done. For example, the ACC may send information to the PFC or presupplementary motor area to cognitively resolve the conflict while it informs other neurons in the brain stem or other autonomic areas to handle primary functions such as heart rate or blood pressure (12).

The problem with this theory is that it doesn't consider some evidence found by electrophysiological methods that the ACC can have an evaluative function.

5.2. The electrophysiological studies

The Electrophysiological studies are mainly done by electroencephalography (EEG) and/or electromyography (EMG). EEG studies showed for the first time the error detection function of the ACC. Rabbitt was the first scientists that mentioned the idea of ERNs in the context of error detection (13). An ERN or error-related negativity is thought to be generated by the ACC whenever an error occurs. There are two major types of ERNs: the response ERN and the feedback ERN. The response ERN takes place when a subject realizes a mistake was done, whereas the feedback ERN is produced when a feedback from the error is sent to the subject. If the subject is not aware of an error and no feedback occurs, the subject will not generate and ERN (6).

Inside the ACC, the ERN is produced at two places: the first one is in the rostral ACC and is specific to errors. The other one, from the caudal ACC and the presupplementary motor area also includes feedback errors (8). The best way to obtain an ERN is to focus on speed but not accuracy, so that it is impossible for a subject to respond everything correctly (7). Therefore, there will be errors and ERNs to study. Moreover, only adults can be tested in ERN studies because ERNs begin to develop along with other cognitive processes in adolescence and adulthood (13).

The ERN represents a difference between expected and actual actions. When an intended action does not take place, the brain reacts in resetting the action or refocusing attention which will slow down the next responses, produce emotional frustration and generate an ERN. This ERN generation after a discrepancy between intended and actual action is known as the reinforcement learning theory (13) stated above. This theory claims that when the ACC receives conflicting information, it redirects this information to other areas in the brain, including the motor areas so that the intended action can be obtained (14). It is assumed that dopamine is highly involved in this circuit. When an error or a "worse-than-expected" event occurs, dopamine neurons are activated saying that the intended action did not happen and that the action produced is worse that what was expected therefore sending a message to the ACC to correct the event (7).

The reinforcement theory is for now the most inclusive theory on the ACC. In this theory, the ACC "detects, monitors errors, evaluates the degree of the error, and then suggests an appropriate form of action to be implemented by the motor system" (14). Thus, the ACC does more than detecting and monitoring errors. It has also an evaluative function which allows it to provide enough information to other parts of the brain to execute a suitable action.

6. Conclusion

The anterior cingulate cortex is an area in the brain involved in errors that has four main functions: executive, evaluative, cognitive and affective. The connections of the

ACC allow it to perform different tasks including detecting and monitoring errors, and sending relevant information to the areas that need to correct the error. These functions are explained by two theories: the conflict monitoring theory and the reinforcement learning theory. Both of these theories contain problems but the reinforcement learning theory includes more evidence and therefore is to this day the one that explains best the functions of the ACC.

Many things have been discovered on the anterior cingulate cortex from the beginning of error processing in the mid 1960s until now. However, much more still needs to be learned, especially about the relation between the affective and cognitive part of the ACC and its connections with the rest of the brain.

References

1. Allman JM, Hakeem A, Erwin JM, Nimchinsky E, Hof P (2001) The anterior cingulate cortex. The evolution of an interface between emotion and cognition. Ann NY Acad Sci 935:107–117

2. Bush G, Luu P, PosnerMI (2000) Cognitive and emotional influences in anterior cingulate cortex. Trends Cogn Sci 4:215–222.

3. Carter, C.S. et al. (2000) Parsing executive processes: strategic vs. evaluative functions of the anterior cingulate cortex. Proc. Natl. Acad. Sci. U. S. A. 97, 1944–1948

4. Critchley, H.D. et al. (2003) Human cingulate cortex and autonomic control: converging neuroimaging and clinical evidence. Brain 126, 2139–2152

5. Devinsky O, Morrell MJ, Vogt BA. (1995) Contributions of anterior cingulate cortex to behaviour. Brain 118: 279-306.

6. Ferrez, P. (2007) Thesis: Error-related EEG potentials in brain-computer interfaces. EPFL, Lausanne

7. Holroyd CB, Coles MGH (2002) The neural basis of human error processing: Reinforcement learning, dopamine, and the error-related negativity. Psychol Rev 109(4):679-709.

8. Kiehl, K.A. et al. (2000) Error processing and the rostral anterior cingulate: an event-related fMRI study. Psychophysiology 37, 216–223

9. Mayberg, H. S. et al. (1999) Reciprocal Limbic-Cortical Function and Negative Mood: Converging PET Findings in Depression and Normal Sadness. American J. Psychiatry 156:675–682

10. Pandya DN, Yeterian EH (1996) Comparison of prefrontal architecture and connections. Philos Trans R Soc Lond B Biol Sci 351:1423–1432

11. Sarter M., Gehring w. J., Kozak R. (2006) More attention must be paid: The neurobiology of attentional effort. Brain Research Reveiws 51 145–160

12. Swick D, Turken AU. (2002) Dissociation between conflict detection and error monitoring in the human anterior cingulate cortex. Proc Natl Acad Sci USA 99: 16354–9.

13. Taylor SF, Stern ER, Gehring WJ. (2007) Neural systems for error monitoring: recent findings and theoretical perspectives. Neuroscientist 13: 160–72.

14. Wikipedia, the free encyclopedia: the anterior cingulated cortex, (2008) <http://en.wikipedia.org/wiki/Anterior_cingulate_cortex>

Table of figures

Figure 0* The anterior cingulate cortex…………………………..………………………1
Figure 1 Medial surface of left cerebral hemisphere..3
Figure 2 A pair of spindle cells in human anterior cingulate cortex……………………..…4
Figure 3 The prefrontal and the limbic system 5
Figure 4 Error-related negativity...7

*Cromie W. J., Discovering how we appreciate a loss. Harward University Gazette. (Dec 2004) <http://www.hno.harvard.edu/gazette/2004/12.09/09-brain.html>