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Original Research

Quality of Life, Psychological Stress, and Cognitive Decline Post-Ruptured Anterior Communicating Artery Aneurysm Endovascular Treatment

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ABSTRACT

Objective: Neuropsychiatric impairment is frequently seen after the treatment of anterior communicating artery aneurysm rupture. The study assessed depression, quality of life, and cognitive function in patients who underwent coiling for anterior communicating artery aneurysm rupture.

Materials & Methods: A retrospective sample of patients with ruptured anterior communicating artery aneurysms treated at our facility were enrolled from the timeframe of August 2018 and October 2021. This research includes 60 individuals who had coil treatment in total. They all finished the QoL and cognitive follow-up surveys. The core aim of the questionnaire was to evaluate each participant's cognitive impairments and depressive symptoms. To determine baseline clinical state, retrospective reviews of patient charts were conducted along with demographics, postoperative course, and specifics of endovascular coiling.

Results: There were 22 females and 38 males. The presentation lasted anything from six months to three years, with most of it taking place in a single year. Of those who experienced post-coiling neurological impairments, 27% had none, and 73% had none. While 38% had no symptoms, 21% had mild depression, 20% had moderate depression, and 21% had severe depression symptoms. 62% of patients experienced depressive symptoms and a decline in cognition following therapy for ruptured ACoA aneurysms. The striatum, ventromedial prefrontal (orbitofrontal) cortex, frontal cortex, and other traumatized anterior brain regions may be the source of these symptoms, which are specific to ACoA-related aneurysms.

Conclusion: Following therapy for ruptured AComA aneurysms, 62% of patients experienced cognitive deficits and depressive symptoms. The difficulties specific to aneurysms associated with AComA that result from injury to anterior brain areas such as the striatum, ventromedial prefrontal (orbitofrontal) cortex, or frontal cortex may be the source of these symptoms.

Keywords: Cognition, Endovascular, ACoA Syndrome, Quality of Life, Psychology, Distress.

Abbreviations: ACA: Anterior Cerebral Artery. ACoA: Anterior communicating Artery. ACoAA: Anterior communicating artery aneurysm. ACC: Anterior cingulate cortex. aSAH: Acute Subarachnoid Hemorrhage. CT: Computed Tomography. CTA: Computed Tomography Angiography. CES-D: Center for Epidemiologic Studies Depression Scale. EVT: Endovascular Treatment. EVD: External Ventricular Drain. fMRI: Functional Magnetic Resonant Imaging. H & H: Hunt and Hess. ISAT: International Subarachnoid Aneurysm Trial. MRA: Magnetic Resonant Angiography. mRS: Modified Rankin Scale. MCC: Middle Cingulate Cortex. PCC: Posterior Cingulate Cortex. QoL: Quality of Life. rCBF: Regional Cerebral Blood Flow. SAH: Subarachnoid hemorrhage. TICS-M: Modified Telephone Interview for Cognitive Status.

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INTRODUCTION

Meningeal signs, headache, unconsciousness, and abnormal neurological functions are some of the clinical indications of subarachnoid hemorrhage (SAH). A cerebral aneurysm rupture is the most frequent cause of SAH. The most prevalent intracerebral aneurysms are those in the anterior communicating artery (ACoA), which also happens to be the main source of aneurysmal subarachnoid hemorrhage. Endovascular coil embolization for treating ruptured intracranial aneurysms gained popularity when the International Subarachnoid Aneurysm Trial (ISAT) results were released in 2002.[1]

SAH or ruptured aneurysms are more common in younger people, and as a result, their psychosocial implications may impede daily functioning for years. Many patients experience increased anxiety years after the SAH event due to brain injury, which causes distraction, focus issues, unhappiness, and a lack of purpose.[2] Anterior communicating artery ruptured aneurysms are considered to be associated with frontal lobe syndrome, also referred to as a dysexecutive syndrome. This is characterized by symptoms like changes in personality, emotional changes, and impairments in executive function (such as diminished self-direction and self-control, psychological instability, apathy, agitation, and excitability, and a lack of criticism, a lack of inhibition in expressing emotions, socially unacceptable behavior, and a disregard for social norms).[2]

Since the aneurysm's location may affect perfusion and metabolism in certain brain regions, the resulting cognitive deficits may be connected to that area. Numerous arterial branches of the ACoA supply blood to the basal forebrain, frontal lobe, anterior cingulate gyrus, septal nuclei, fornix, genu of the corpus callosum, and other neuroanatomical tissues. Amnesia, confabulation, personality disorders, and disturbance to both recent and distant memory were previously identified as the main indicators of ACoA aneurysm rupture. Both intraoperative difficulties, particularly aneurysms associated with ACoA, and compromised anterior brain regions, such as the frontal cortex, ventromedial prefrontal (orbitofrontal cortex), or striatum, may contribute to these symptoms.[3]

The research on the quality of life and long-term functional outcomes of ruptured ACoA aneurysms in this group of populations is scarce. There is currently a significant lack of information on the cognitive sequelae following aneurysmal SAH, in contrast to the more often investigated clinical and surgical outcomes following treatment. According to prior investigations, patients with surgically operated ACoA aneurysms have been found to suffer memory and cognitive impairment. Neuropsychological evaluations of ISAT patients revealed a decreased risk of cognitive impairment, which has been linked to depression and a lower quality of life (QoL) in endovascular coiling. It is well known that these people's cognitive profiles vary with time, even though long-term cognitive and QoL outcomes across various treatment strategies have not yet been reported. The purpose of this study was to evaluate the effects of endovascular coil embolization on patients with ruptured ACoA aneurysms in terms of their quality of life and cognitive function.

MATERIAL AND METHODS

Study Design & Setting

At our institution in Pakistan, the dedicated neuro-interventional department conducted this single-center retrospective follow-up study. We looked at patients who were admitted to our hospital; Lahore General Hospital, Department of Diagnostic and Interventional Radiology between August 2018 and October 2021 with ruptured ACoA aneurysms. After being made aware of the goal of the study, all patients gave their agreement to be a part of the evaluations and analysis.

Inclusion Criteria

The following were the prerequisites of the study: (1) SAH due to an ACoA aneurysm rupture, as determined by CT scanning, followed by CT angiography or digital subtraction angiography, (2) coiling to treat the ruptured aneurysm, (3) the absence of significant post-procedural complications (such as a post-operative coma or hematoma), and (4) functional recovery enabling the patient to answer all of the detailed questions.[4] Postoperative follow-up with subsequent CTA or MRA.

Exclusion Criteria

The following were the exclusion criteria: (1) a Hunt and Hess grade of 4–5, (2) a history of a neurological or psychiatric condition, (3) cognitive deficits before the SAH, and (4) major complications following the surgery, and (5) an unwillingness to cooperate in cognitive tests.

Data Collection

A total of 60 participants were included in the study, prospectively. The survey mostly used in literature to identify depression is CES-D (Centre for Epidemiological Studies for Depression).[6]

Results of 16 or above indicate persons who are more likely to experience depression. One of our researchers used the Telephone Interview for Cognitive Status-Modified (TICS-M) questionnaire to evaluate the patients who gave their consent to participate in terms of their overall cognitive status. Cognitive impairment is indicated by a score of 27 or less.[7] We investigated both questionnaires in detail and revised them into our questionnaire which was simple and according to our patient's educational level. Most of our patients were illiterate so we needed to help them understand the questions, and also asked attendants to help them. After analyzing the results of these tests, we created our anterior circulation syndrome questionnaire. Additional classifications are made as mild, moderate, and severe based on their symptoms.

Chart Review

All 60 patients' charts were examined. Age, sex, baseline clinical parameters, H&H Grade, aneurysm site, and size were among the demographic factors highlighted. We also noted those cases where external ventricular drain (EVD) was done before aneurysm treatment. For each procedure, we additionally noted whether an intraoperative aneurysm ruptured, intraoperative vasospasm or the perforators or ACA were occluded after coiling. Post-coiling residual aneurysm, other post-procedural complications such as hydrocephalus, meningitis, stroke, hematomas visible on post-procedural imaging, vasospasm, hemiplegia, and post-procedural rupture, were also covered in the data. Any postoperative EVD re-insertions and any repeated aneurysm treatment were also reported. We gathered data on hospital discharges, including a modified Ranking Scale (mRS). The modified Ranking Scale was established retrospectively using all of the readily available chart data. We also provide information on the follow-up period, which was calculated as the number of months

between the patient's last contact and the date of hospital admission.

RESULTS

Population

60 patients were treated at our facility between August 2018 and October 2021 for ruptured ACoA aneurysms with Hunt and Hess grades of 1 to 3. All of the cases met the inclusion criteria and a post-procedure follow-up that lasted longer than six months was done.

Age & Gender Distribution

The median patient age was years (between 20 and 70 years), with 22 patients (37% female) and 38 patients (63%) male.

Outcome

All patients were treated with endovascular procedures. The cognitive evaluation was done on all of the enrolled patients. The procedure and assessment took an average of 12 months to complete (ranging from 6 to 36 months). Among a cohort of 60 patients, twelve (21%) patients were found to have severe Anterior circulation syndrome, twelve (21%) of them had moderate symptoms, and eleven patients (20%) had mild symptoms. Twenty-one (38%) do not have any symptoms of anterior circulation syndrome despite a ruptured ACoA aneurysm treated with coiling. Most patients who suffered from frontal lobe symptoms were in the age group of 50 to 60 years. The largest number of patients (21) presented with symptoms within 6 to 12 months duration post coiling and the initial 6 months. The presence of hemorrhage, aneurysm size, association with co-morbidities, treatment modality (endovascular coiling), anatomy of the anterior cerebral artery, aneurysm projection, and neurological deficits were also recorded, they were not significantly associated with cognitive impairment and depression. Only 15 of them (27%) have some neurological deficit exhibited in post post-coiling follow-up period. 11 of them have difficulty walking, 2 of them have headaches, the same number have vertigo and three of them have visual problems. Follow-up magnetic resonant angiogram was carried out in most of the cases with institutional protocol after 6 months of the initial coiling procedure. Only 2 cases showed recurrence, and 4 of them have a stable residual neck (Figure 1 a-d).

According to the statistical analysis, the male gender was independently associated with anterior circulation syndrome in our study cohort.

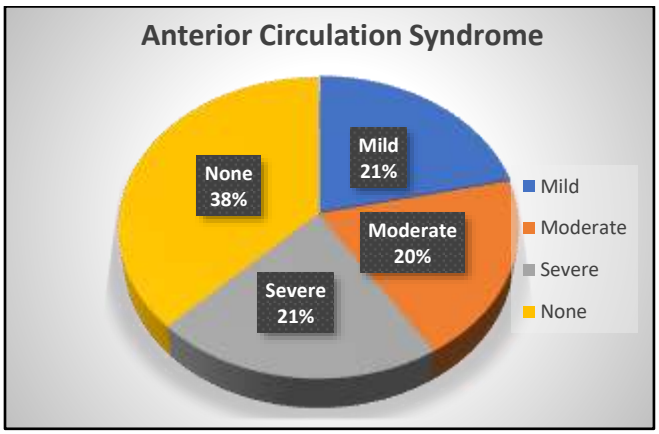
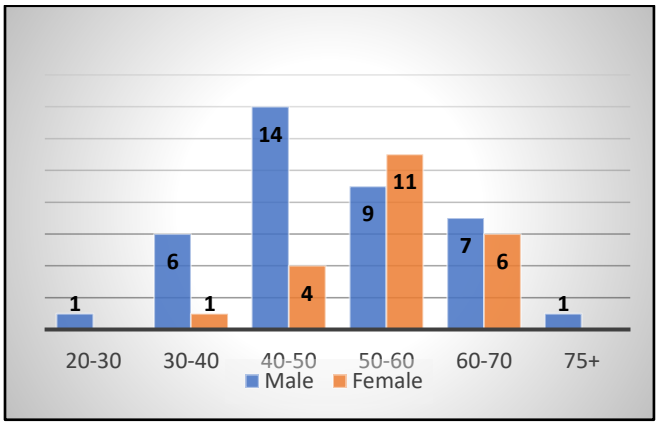


Figure 1a:



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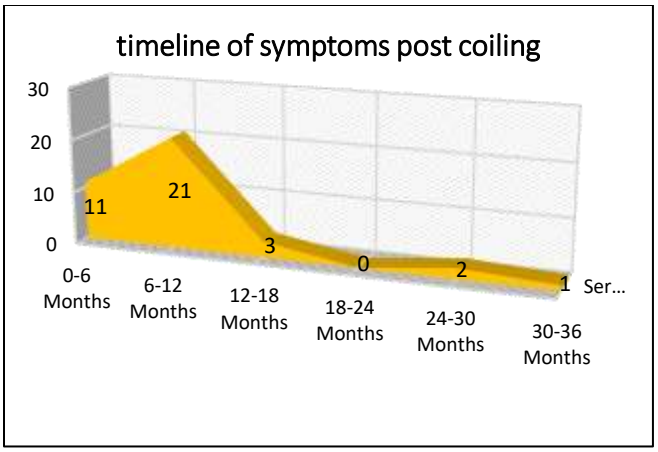

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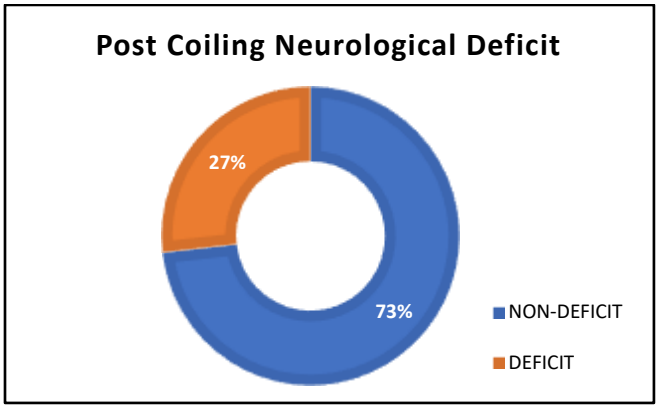

Figure 1 d

Figure 1 (a-d): Figures showcasing data of ACoA post-coiling cases: a) Grading of Anterior Circulation Syndrome, b) Age groups and gender distribution, c) Timeline of appearance of symptoms post EVT treatment & d) Incidence of neurological deficits in post-EVT treated cases of AComA.

DISCUSSION

A patient's quality of life, ability to work, and participation in social activities are all negatively impacted by cognitive impairment. There isn't any research that specifically examines how young people with good-grade SAH manage. ACoA aneurysm rupture and treatment are more commonly linked to cognitive and behavioral impairments than aneurysms in other locations, and ACoA aneurysms are among the most often identified ruptured aneurysms.[3]

We have conducted our study to find out the relationship between ruptured ACoA aneurysm treated with EVT and behavioral changes. The Mini-Mental State Examination for Cognitive Functions and the Center for Epidemiology Studies-Depression questionnaire were used in our study to evaluate cognitive functioning.[6] According to our findings, 62% of patients treated with coiling after ruptured ACoA aneurysms had depressive symptoms. Between 5% and 50% of those who have experienced SAH are affected by depression and it lasts up to 18 months, in contrast to many other cognitive functions that become better with time. Depression that remained after SAH may have been brought on by the terrifying event and fear of reliving it. It has been demonstrated that neurosurgical techniques, mood, anxiety, sleep, and exhaustion all have an impact on cognitive and functional outcomes.[2]

Personality disorder is a very common finding in ruptured ACoA aneurysms treated either surgically or with coiling. To understand this association, we need to look at the anatomy of the anterior communicating artery and its relation to anatomical structures. Traditional, simple intracranial bifurcation aneurysms are not equivalent to ACoA aneurysms. The ACoA, the A1 and A2 segments of the bilateral anterior cerebral arteries, and the bilateral anterior cerebral arteries constitute a complex of five arteries that contain them. Seven other arteries, including the bilateral frontopolar artery, the bilateral orbitofrontal artery, and the bilateral recurrent arteries, surround the ACoA complex (recurrent artery of Heubner). The gyrus rectus is superior to ACoA. The inferior frontal gyrus, which lies next to the gyrus rectus, is linked to personality changes, confabulation, and anterior communicating artery aneurysmal amnesia when it ruptures. This condition is known as ACoA syndrome.[8] Understanding the relationship between ACoA and perforating branch vessels is essential. The ACoA perforating branches, which are almost always present, supply blood arteries to the intracranial hypothalamus and optic chiasm, two

very important functional regions. After an ACoA aneurysm is surgically clipped or embolized, side effects include personality changes, mental disorders, mutism, and even internal environment disruption may appear. The main reason for this is that during the surgery, several of the ACoA's perforating branches sustained injury. The posterosuperior region of the ACoA gives rise to the subcallosal branch. With branches leading to the septum pellucidum, anterior hypothalamus, anterior cingulate gyrus, anterior commissure, and lamina terminalis, it extends in the direction of the corpus callosum. Additional perforators include the hypothalamus and optic chiasm branches. The hypothalamus and subcallosal branches must be saved during endovascular treatments.[5]

Furthermore, to understand the complex relationships, we need to look at the research by Leodante da Costa et al, which demonstrated how aSAH compromises long-term hippocampal potentiation, a crucial aspect of learning and memory. Our capacity to shift our attention from one activity to another and to stop willful behavior and improper activities is referred to as the executive function (error monitoring). The inhibitory control test gives a close assessment of working memory ability. Inhibitory control is a fundamental component of executive function. When performing an inhibitory task, the intention must be to keep the appropriate response in working memory. Working memory tasks were linked to a broad increase in cortical activity in a study that was undertaken. They also found a negative correlation between anterior cingulate gyrus connectivity and cognitive results. The ACC consists of cognitively demanding and motor planning processes that are linked to effective and emotional responses. The electrophysiological phenotype for neurocognitive impairment in this population may be increased activity in this complex area engaged in network modulation and integration between motor control, behavior, and effect. They are unable to distinguish between upregulation driven by aneurysm rupture or compensatory mechanisms as the cause of the enhanced activity.[4]

Furthermore, we need to understand the connections between the regions supplied by perforating branches of ACoA as when these connections are severed during treatment or aSAH results in cognitive decline and depression. Intense cognitive conflict may be detected by the anterior cingulate cortex, which may also have a specific role to play in the suppression of the memory of experienced events. The purpose of the ACC is to produce erroneous responses to experimental events.[9] This links to personality disorders experienced by patients of ruptured ACoA aneurysms. The "cognitive" prefrontal cortex and the "emotional" limbic system are both connected to the anterior cingulate cortex (ACC, which occupies a unique location in the brain. Previously, the ACC anatomy was discussed. Vogt asserts that this literature makes use of the ACC and MCC jargon (Figures 2 a & b).

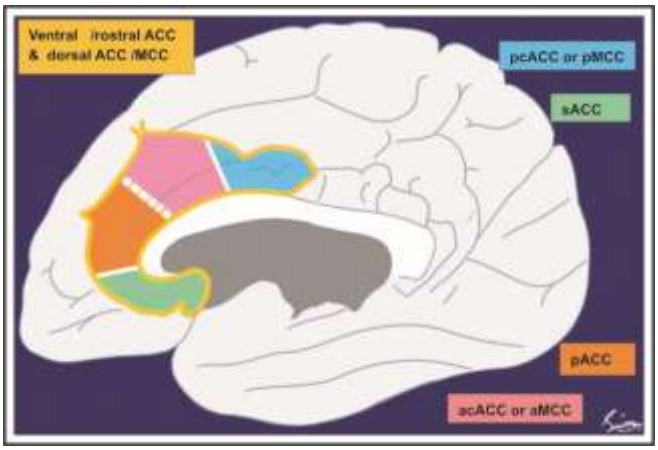

Figure 2 a: Anatomy of ACC described by Brodmann, further expanded by Vogt's System.
Key: ACC: Anterior Cingulate Cortex, MCC: Middle Cingulate Cortex, aMCC: Anterior Middle Cingulate Cortex, pMCC: Posterior Middle Cingulate Cortex, sACC: Subgenual Anterior Cingulate Cortex, pACC: Pregenual Anterior Cingulate Cortex

This area contains von Economo neurons (spindle neurons), which are generally restricted to the cingulate (ACC and MCC) and insular cortices.

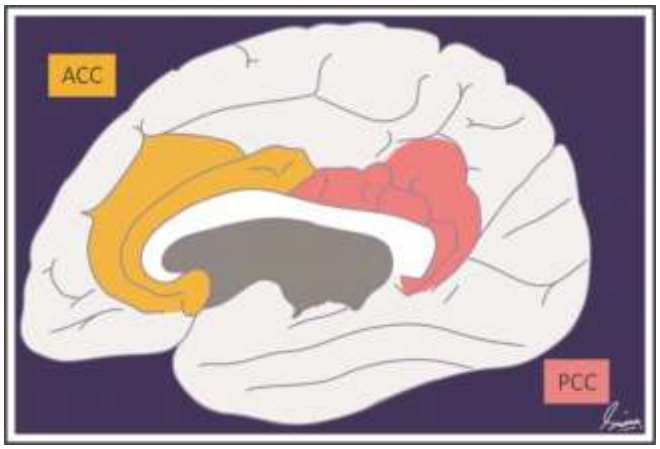

Figure 2 b: Anatomy of ACC described by Brodmann, further expanded by Vogt's System.

Key: ACC: Anterior Cingulate Cortex, PCC: Posterior Cingulate Cortex

Figure 2 a & b (Appropriated figure [10]): Anatomy of ACC described by Brodmann, further expanded by Vogt's System.

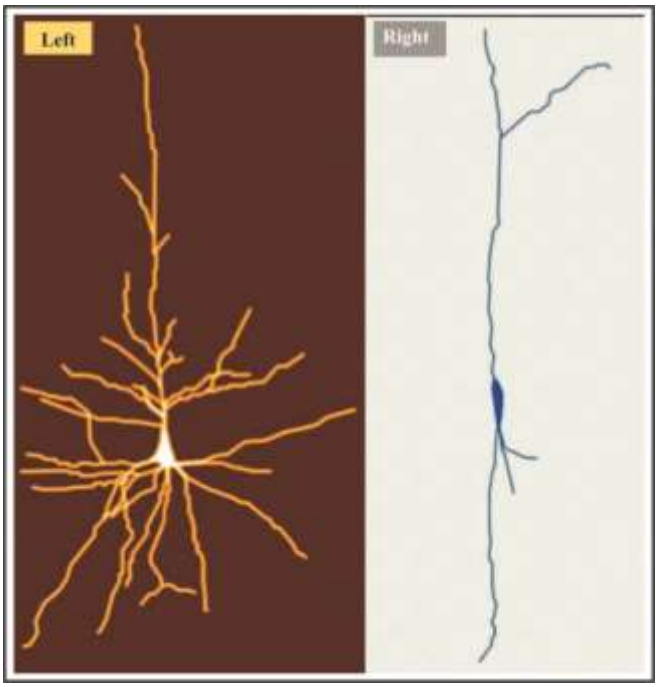

Figure 3: Appropriated figures [10]:(Left): Both humans and great apes have von Economo (spindle) neurons. They are located in the insula and cingulate cortex of humans. With an average volume more than four times that of pyramidal neurons, they are large projection neurons. In addition, the apical and basal dendrites of these neurons differ significantly from those of pyramidal neurons in that they are longer and have fewer branches. It has been proposed that larger sizes might represent longer connections and faster conduction times. (Right): A pyramidal neuron is illustrated for comparison.

No other mammal has von Economo neurons; only humans and great apes do. They are more prevalent in humans, which may have been advantageous for evolution. Because they are substantially bigger than pyramidal neurons, they probably have more connections across different sections of the brain and can transmit information more quickly. Von Economo neurons provide an adaptive role by allowing humans and big apes to respond spontaneously and intuitively in social circumstances (Figure 3).

The brainstem monoamine nuclei and the Brodman area 9 of the thalamus are two areas of the brain to which most or all of the cingulate cortex is related. The amygdala, lateral hypothalamus, brain stem regions, the hippocampus region, and regions involved in reward (orbitofrontal cortex, ventral striatum), memory, and autonomic processes are all strongly connected to the ACC in this area. The cingulate cortex projects to the prefrontal cortex as well as the amygdala. They only found a link between emotional awareness and activity in the MCC when emotional inputs were extremely powerful and psychologically arousing. Overactive PCC and MCC are involved in most anxiety disorders. In conclusion, the cingulate cortex plays a critical role in reducing the emotional impacts of cognitive processes (Figure 4).

The limbic and cingulate cortex systems are involved in emotion, behavior, and memory. Anterior cingulate cortex connections can be observed in primate brain views. Although there are connections in both ways, the arrows indicate the primary direction of connectivity. Both the supracallosal anterior cingulate cortex and the pregenual cingulate cortex, particularly from the lateral orbitofrontal cortex and the medial/mid-orbitofrontal cortex, are connected. The anterior cingulate cortex is connected to the amygdala, the visual and auditory cortex in the superior temporal

sulcus, and the (auditory) superior temporal gyrus (STG) of the temporal lobe.

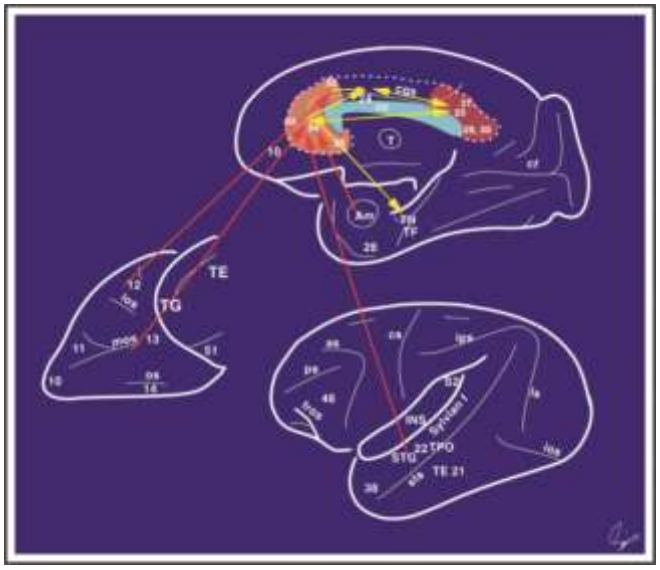

Figure 4: (Appropriated figure [11], Used with permission)**:** Connections of the anterior cingulate cortex.

Key (Figure 4):
as: arcuate sulcus; cc: corpus callosum; cf: calcarine fissure; cgs: cingulate sulcus; cs: central sulcus; ls: lunate sulcus; ios: inferior occipital sulcus; mos: medial orbital sulcus; os: orbital sulcus; ps: principal sulcus; sts: superior temporal sulcus; sf: Sylvian (or lateral) fissure; Am: Amygdala; INS: Insula; TE (21): inferior temporal visual cortex; 38, TG, temporal pole cortex; 13, 11, medial orbitofrontal cortex; TPO: multimodal cortical area in the superior temporal sulcus; TF and TH: parahippocampal cortex; and STG (22): superior temporal gyrus auditory association cortex; 23, 31 posterior cingulate cortex; 29, 31 retrosplenial cortex; 51 olfactory (prepyriform and periamygdaloid) cortex.

As was previously mentioned, several psychopathologies seem to be related to the over- or under-activation of particular sub-regions. This is not shocking considering that several mental illnesses have a poor ability to adjust to the effect. We may be able to better understand the pathophysiology and potential treatments if we grasp the precise roles that the various functional sub-regions play in the regulation of emotions.[10] We believe that these complex connections are interrelated and responsible for behavioral changes in ACoA ruptured aneurysm cases. The findings of our exploratory investigation highlight the significance of carrying out follow-up research that assesses long-term effects using validated daily functioning measures when choosing a therapeutic strategy for ruptured AcomA aneurysms.

CONCLUSION

The data support a novel interpretation of the relationships and roles of the cingulate cortex in emotion, action, and memory. The anterior cingulate cortex receives information regarding unrewarding and rewarding outcomes from the orbitofrontal cortex. To the posterior cingulate cortex, parietal cortical areas transmit information about actions and spatial orientation. The cingulate cortex is thought to be able to act-outcome learn as a result of these inputs and outputs from the midcingulate motor area to the premotor areas. Additionally, because both contain links to the hippocampus system, the anterior cingulate cortex is active in emotion while the posterior cingulate cortex is active in memory. Since perforators in the ACoA region supply these essential structures, evidence from numerous investigations has led to this conclusion. Thus, during endovascular or microsurgical treatments for ACoA aneurysms, care must be given to protect these perforators, and further prospective studies are needed to fully understand these complex connections.

RECOMMENDATIONS

Cerebral Vasospasm and inadvertent occlusion of anterior communicating artery perforators may occur after coil embolization of ruptured cerebral aneurysms. The damage to these perforators should be considered in patients who develop inept, depression, and cognitive decline after treatment. Further large-scale studies are warranted to describe all aspects of Anterior Communicating artery Syndrome in post-coiling patients.

LIMITATIONS OF THE STUDY

One of the major limitations of our study is the lack of comparison of both coiling and clipping groups treated with an Anterior communicating artery aneurysm. Another limitation is the lack of availability of post-coiling MRI in all patients to look for ischemic damage. Pre and post-MRI scans would have solidified the research by showcasing the development of ischemic damage in a more objective and scientific context, however, due to lack of availability and high cost in our country they could not be conducted.

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Additional Information

The abstract has been previously presented at the WFITN Kyoto Conference 2022.
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Human Subjects: Waiver of Consent was obtained from the ethical review board.
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Data Availability: Data will be made available upon an adequate request by the principal author SA (masterinfluencer@gmail.com)
Other Relationships: All authors declare that there are no other relationships or activities that could appear to have influenced the submitted work.

AUTHORS CONTRIBUTIONS

Sr#	Author's Full Name	Intellectual Contribution in Manuscript:
1.	Saima Ahmad	study design and methodology, paper writing, analysis of data, and interpretation of results.
2.	Hira Jamil	Data collection and calculations.
3.	Muhammad Ajmal Khan	Literature review and referencing.