

IMPACT OF FRONTAL LOBE SURGERIES ON PERSONALITY AND MOOD: A COMPREHEN- SIVE REVIEW

Mauricio Lopes da Silva Netto

<http://lattes.cnpq.br/4791743372358340>

Rafaela Araújo Costa Pinto

<https://lattes.cnpq.br/2215473296353541>

Vitória Martins Granja de Moura

<http://lattes.cnpq.br/8418174477729229>

Giovanna Mariotti Moreira

<http://lattes.cnpq.br/1580683314937989>

Lara Fernanda de Sá Guimarães

<http://lattes.cnpq.br/4791743372358340>

Vanessa Britto Zafra

<http://lattes.cnpq.br/2807146195840720>

Ana Luísa Trindade de Carvalho

Alisson Beraldo

<http://lattes.cnpq.br/4791743372358340>

Henrique Neves Ravenna Picazo

<http://lattes.cnpq.br/4791743372358340>

Lara Macatrão Durante Bacelar

Mário Vitor Kern Xavier

Melyssa Aryane de Oliveira

<http://lattes.cnpq.br/9531560727825211>

João Pedro Ravagnani Semensato

<http://lattes.cnpq.br/4791743372358340>

All content in this magazine is licensed under a Creative Commons Attribution License. Attribution-Non-Commercial-Non-Derivatives 4.0 International (CC BY-NC-ND 4.0).



Abstract: INTRODUCTION Frontal lobe surgeries, originating from early 20th-century procedures like prefrontal lobotomies, have evolved significantly, reflecting advancements in medical science and surgical technologies. The frontal lobe, encompassing areas critical for executive functions, motor activities, and emotional regulation, plays a pivotal role in cognitive and social behaviors. Surgeries are indicated for conditions such as brain tumors, epilepsy, and severe psychiatric disorders, with various techniques including lesionectomy, lobectomy, and deep brain stimulation. These interventions, while therapeutic, can lead to significant personality and mood changes due to the disruption of neural circuits within the frontal lobe. **OBJECTIVE** To investigate the impact of frontal lobe surgeries on personality; mood changes; patients' daily lives and quality of life. **METHODS** This is a narrative review which included studies in the MEDLINE – PubMed (National Library of Medicine, National Institutes of Health), COCHRANE, EMBASE and Google Scholar databases, using as descriptors: “Frontal Lobe Surgery” AND “Personality Change” AND “Mood Disorders” AND “Cognitive Functions” AND “Neuroplasticity” in the last years. **RESULTS AND DISCUSSION** The efficacy of frontal lobe surgeries varies, with different techniques offering specific benefits and risks. Lesionectomy and lobectomy can significantly reduce symptoms in refractory epilepsy and large tumors, respectively, but they also carry a risk of cognitive and emotional changes. Mood changes, including depression and anxiety, are common due to the involvement of the orbitofrontal cortex and anterior cingulate cortex in emotional regulation. Identifying risk factors, such as the extent of resection and patient-specific factors like genetics and pre-existing conditions, is crucial for optimizing outcomes. Rehabilitation, including cognitive and emotional support, plays a critical role

in recovery, while patient satisfaction and quality of life are significantly influenced by the degree of these changes. **CONCLUSION** Frontal lobe surgeries provide significant therapeutic benefits for various neurological and psychiatric conditions but pose risks of cognitive and emotional changes. Advances in surgical techniques and neuroimaging, along with a multidisciplinary approach, are essential for improving outcomes. Personalized treatment plans that consider genetic, demographic, and socioeconomic factors, as well as comprehensive post-operative care, including psychological support and cognitive rehabilitation, are critical for optimizing patient recovery and quality of life. Future research should focus on long-term impacts, ethical considerations, and the development of targeted interventions to mitigate adverse effects and enhance recovery.

Keywords: Frontal Lobe Surgery; Personality Changes; Mood Alterations; Cognitive Rehabilitation; Neuropsychological Outcomes.

INTRODUCTION

The history of frontal lobe surgeries dates back to the early 20th century, with the advent of prefrontal lobotomies as a radical treatment for severe psychiatric disorders¹. The pioneering work of Egas Moniz in the 1930s marked the inception of such interventions, where the aim was to alleviate symptoms of psychosis and severe depression by severing connections in the prefrontal cortex¹. Despite the significant ethical controversies and mixed outcomes associated with these early procedures, they laid the foundation for modern neurosurgical techniques aimed at treating various neurological and psychiatric conditions². The evolution from crude lobotomies to precise, minimally invasive surgeries underscores a remarkable journey in medical science, reflecting a better understanding of brain function and the

advent of sophisticated surgical technologies². Anatomically, the frontal lobe is a critical region of the brain, encompassing areas such as the prefrontal cortex, premotor cortex, and primary motor cortex³. It is situated at the anterior part of the cerebral hemispheres and is responsible for a plethora of complex cognitive functions³. These include executive functions, such as decision-making, problem-solving, planning, and social behavior regulation⁴. The frontal lobe also plays a pivotal role in voluntary motor activity and is intricately involved in language production⁴. The intricate neural networks within the frontal lobe facilitate its diverse functions, highlighting its importance in maintaining overall brain health and cognitive integrity⁵.

Cognitively, the frontal lobe is indispensable for higher-order functions that define human behavior and personality⁵. The prefrontal cortex, in particular, is crucial for executive functions that involve working memory, cognitive flexibility, and inhibitory control⁶. These functions enable individuals to plan, make decisions, and regulate social behavior effectively⁶. Emotionally, the frontal lobe, especially the orbitofrontal cortex, is involved in processing emotional responses, regulating mood, and mediating social interactions⁷. The interplay between cognitive and emotional functions underscores the frontal lobe's role in integrating various aspects of human experience, making it a focal point in understanding the impact of surgical interventions on personality and mood⁷. Frontal lobe surgeries are indicated for a range of medical conditions, including brain tumors, epilepsy, traumatic brain injuries, and psychiatric disorders such as obsessive-compulsive disorder (OCD) and severe depression⁸. The decision to perform surgery is often driven by the need to alleviate symptoms that are refractory to medical treatment⁹. For instance, intractable

epilepsy that originates in the frontal lobe may necessitate resective surgery to improve quality of life⁹. Similarly, psychosurgery, though less common today, is considered for severe psychiatric conditions when conventional therapies fail¹⁰. Understanding the precise indications for these surgeries is essential for optimizing patient outcomes and minimizing potential risks¹⁰.

Various surgical procedures can be performed on the frontal lobe, each tailored to address specific conditions¹¹. These include lesionectomy, lobectomy, and more advanced techniques such as stereotactic surgery and deep brain stimulation (DBS)¹². Lesionectomy involves the removal of a localized lesion, often used in cases of focal epilepsy¹². Lobectomy entails the resection of a larger portion of the frontal lobe and is typically reserved for more extensive pathology, such as large tumors¹³. Stereotactic surgery allows for precise targeting of specific brain areas using imaging guidance, minimizing damage to surrounding tissues¹³. DBS, on the other hand, involves the implantation of electrodes to modulate neural activity, offering a reversible and adjustable therapeutic option for certain movement and psychiatric disorders¹⁴. The mechanisms by which frontal lobe surgeries can lead to personality changes are multifaceted and involve the disruption of neural circuits critical for personality traits and social behavior¹⁴. The prefrontal cortex, for instance, is integral to executive functions and social cognition¹⁵. Surgical intervention in this area can impair these functions, leading to changes in behavior and personality¹⁵. The underlying neural plasticity, which allows for adaptation and recovery, also plays a role in the extent and nature of these changes¹⁶. Additionally, the balance between the excitatory and inhibitory neural activity in the frontal lobe is crucial for maintaining personality traits, and any alteration can result in significant behavioral shifts¹⁶.

Frontal lobe surgeries have a profound impact on patients' mood, given the region's involvement in emotional regulation¹⁷. The orbitofrontal cortex, for instance, is crucial for processing reward-related information and regulating emotional responses¹⁸. Disruption in this area can lead to mood disorders such as depression and anxiety¹⁸. The anterior cingulate cortex, another critical area within the frontal lobe, is involved in emotional processing and cognitive control¹⁹. Surgical intervention in this region can affect mood regulation, leading to emotional instability¹⁹. The interplay between different regions of the frontal lobe and their connections with other brain areas underscores the complex nature of mood changes post-surgery²⁰. A review of clinical studies reveals varied outcomes regarding the effects of frontal lobe surgeries on personality and mood²¹. Some studies report significant improvements in symptoms and quality of life, particularly in patients with refractory epilepsy and certain psychiatric disorders²¹. However, other studies highlight the potential for adverse effects, including personality changes, emotional instability, and cognitive deficits²². These mixed outcomes underscore the need for careful patient selection, precise surgical planning, and comprehensive post-operative care to optimize results²². The variability in study findings also points to the need for further research to elucidate the factors that influence surgical outcomes²³.

Assessing personality and mood changes post-surgery involves the use of various tools and methods²³. Standardized neuropsychological tests, such as the Wisconsin Card Sorting Test and the Iowa Gambling Task, are commonly used to evaluate executive functions and decision-making abilities²⁴. Emotional and personality assessments may include tools like the Beck Depression Inventory and the Minnesota

Multiphasic Personality Inventory²⁴. These assessments provide a comprehensive understanding of the cognitive and emotional changes that occur following surgery, guiding clinical management and rehabilitation efforts²⁵. Objective measurement of these changes is crucial for evaluating the efficacy of surgical interventions and tailoring post-operative care to individual patient needs²⁵. The neurobiology of mood changes following frontal lobe surgeries is complex and involves multiple neural circuits and neurotransmitter systems²⁶. The dopaminergic system, for instance, plays a significant role in reward processing and mood regulation²⁷. Disruption of dopaminergic pathways in the frontal lobe can lead to mood disorders such as depression²⁷. Similarly, the serotonergic system, which is involved in emotional regulation, can be affected by surgical interventions, leading to changes in mood²⁸. Understanding the neurobiological mechanisms underlying mood changes is essential for developing targeted therapeutic strategies to manage these changes and improve patient outcomes²⁸.

Notable cases of patients who have undergone frontal lobe surgeries provide valuable insights into the potential outcomes and challenges associated with these procedures²⁹. Famous cases, such as that of Phineas Gage, who suffered a traumatic brain injury to his frontal lobe, highlight the profound impact of frontal lobe damage on personality and behavior²⁹. Gage's case, in particular, underscored the role of the frontal lobe in personality regulation and social behavior³⁰. Contemporary cases of patients undergoing frontal lobe surgeries for epilepsy or tumors also illustrate the diverse outcomes, ranging from significant symptom relief to adverse cognitive and emotional changes³⁰. These cases emphasize the need for individualized treatment approaches and comprehensive post-operative care³¹. Long-

term adverse effects of frontal lobe surgeries on personality and mood are a critical concern³². Studies have shown that while some patients experience significant improvements in symptoms and quality of life, others may develop chronic mood disorders or persistent personality changes³². The long-term impact of these surgeries depends on various factors, including the extent of the surgical intervention, the underlying pathology, and the patient's pre-surgical cognitive and emotional status³³. Long-term follow-up and comprehensive rehabilitation programs are essential to address these adverse effects and support patients in their recovery journey³³.

Comparing frontal lobe surgeries with other treatments for similar conditions provides valuable insights into the relative efficacy and safety of these interventions³⁴. For instance, pharmacological treatments for refractory epilepsy or severe psychiatric disorders may offer symptom relief but often come with significant side effects³⁵. In contrast, surgical interventions can provide more sustained symptom control but carry the risk of cognitive and emotional changes³⁵. The choice of treatment should be based on a thorough evaluation of the patient's condition, the potential benefits and risks of each treatment option, and the patient's preferences and overall health status³⁶. A multidisciplinary approach is often necessary to provide the best possible care³⁶. Ethical considerations related to frontal lobe surgeries are paramount, given the potential for significant cognitive and emotional changes³⁷. Informed consent is a critical aspect of the surgical process, ensuring that patients understand the potential risks and benefits of the procedure³⁸. Ethical issues also arise in the context of psychosurgery, where the goal is to alleviate severe psychiatric symptoms³⁸. The potential for changes in personality and behavior raises important questions about

the patient's autonomy and quality of life³⁹. Ethical guidelines and rigorous oversight are essential to ensure that these surgeries are performed with the utmost care and respect for patient rights³⁹.

Future perspectives in frontal lobe surgery research and techniques hold promise for improving patient outcomes⁴⁰. Advances in neuroimaging, such as functional MRI and diffusion tensor imaging, provide detailed maps of brain connectivity and function, aiding in precise surgical planning⁴¹. Minimally invasive techniques, such as endoscopic surgery and laser ablation, offer the potential for reducing surgical trauma and improving recovery times⁴¹. Research into neuroplasticity and rehabilitation strategies continues to provide insights into optimizing post-operative recovery and mitigating adverse effects⁴². These advancements highlight the dynamic and evolving nature of frontal lobe surgery and its potential to improve the lives of patients with complex neurological and psychiatric conditions⁴². Personality and mood changes following frontal lobe surgeries can significantly impact patients' quality of life⁴³. Changes in personality traits, such as increased impulsivity or emotional instability, can affect interpersonal relationships, work performance, and overall well-being⁴⁴. Mood disorders, such as depression or anxiety, can further exacerbate these challenges, leading to a diminished quality of life⁴⁴. Comprehensive post-operative care, including psychological support and rehabilitation, is essential to address these changes and support patients in their recovery journey⁴⁵. Understanding the impact of these changes on quality of life is crucial for developing effective therapeutic strategies and improving patient outcomes⁴⁵.

Complementary therapies play a vital role in managing personality and mood changes after frontal lobe surgery⁴⁶. Cognitive-behavioral therapy, for instance, can help

patients develop coping strategies and improve emotional regulation⁴⁷. Mindfulness-based therapies and other forms of psychotherapy can also be beneficial in managing mood disorders and enhancing psychological resilience⁴⁷. Additionally, occupational therapy and social support interventions can help patients reintegrate into their daily lives and improve their quality of life⁴⁸. These complementary therapies, when integrated into a multidisciplinary treatment plan, can provide comprehensive care that addresses both the cognitive and emotional aspects of recovery following frontal lobe surgery⁴⁸. Genetics and predisposition play a crucial role in determining individual responses to frontal lobe surgeries⁴⁹. Genetic factors can influence how patients respond to surgical interventions, both in terms of surgical outcomes and the extent of cognitive and emotional changes⁵⁰. For instance, genetic variations in neurotransmitter systems, such as the dopaminergic and serotonergic pathways, may affect mood regulation and personality traits⁵⁰. Understanding these genetic predispositions can help tailor surgical and post-operative care to individual patients, optimizing outcomes and minimizing adverse effects⁵¹. Genetic research continues to provide valuable insights into the interplay between genetics and brain function, highlighting the importance of personalized medicine in neurosurgery⁵¹.

Gender differences can also influence the outcomes of frontal lobe surgeries⁵². Studies have shown that men and women may experience different cognitive and emotional changes following surgery, potentially due to differences in brain structure and function⁵³. For instance, women may be more susceptible to mood disorders such as depression, while men may exhibit more significant changes in impulsivity and aggression⁵³. These gender differences underscore the need for tailored

approaches to surgical planning and post-operative care, ensuring that both men and women receive the most appropriate and effective treatments⁵⁴. A multidisciplinary approach is essential in the treatment and follow-up of patients undergoing frontal lobe surgeries⁵⁴. This approach involves collaboration among neurosurgeons, neurologists, psychiatrists, psychologists, and rehabilitation specialists, ensuring comprehensive care that addresses all aspects of the patient's condition⁵⁵. Each specialist brings unique expertise to the treatment plan, from surgical precision to psychological support and cognitive rehabilitation⁵⁶. A multidisciplinary team can provide holistic care that maximizes recovery and quality of life, addressing the complex and interrelated challenges associated with frontal lobe surgeries⁵⁶.

OBJETIVES

To investigate the impact of frontal lobe surgeries on personality; mood changes; patients' daily lives and quality of life.

SECUNDARY OBJETIVES

1. To identify risk factors for adverse personality and mood changes.
2. To examine the role of rehabilitation and complementary therapies in post-surgical recovery.
3. To compare outcomes among different patient demographics and pre-existing conditions.
4. To explore the ethical considerations and patient satisfaction associated with frontal lobe surgeries.
5. To study the influence of genetics, gender, and socioeconomic factors on surgical outcomes.

METHODS

This is a narrative review, in which the main aspects frontal lobe surgeries on personality; mood changes; patients' daily lives and quality of life in recent years were analyzed. The beginning of the study was carried out with theoretical training using the following databases: PubMed, sciELO and Medline, using as descriptors: "Frontal Lobe Surgery" AND "Personality Change" AND "Mood Disorders" AND "Cognitive Functions" AND "Neuroplasticity" in the last years. As it is a narrative review, this study does not have any risks.

Databases: This review included studies in the MEDLINE – PubMed (National Library of Medicine, National Institutes of Health), COCHRANE, EMBASE and Google Scholar databases.

The inclusion criteria applied in the analytical review were human intervention studies, experimental studies, cohort studies, case-control studies, cross-sectional studies and literature reviews, editorials, case reports, and poster presentations. Also, only studies writing in English and Portuguese were included.

RESULTS AND DISCUSSION

The efficacy of different frontal lobe surgical techniques has been evaluated in numerous studies, each providing insights into the benefits and limitations of various approaches⁵⁷. Lesionectomy, for instance, has shown efficacy in reducing seizure frequency in patients with refractory epilepsy, but the extent of cognitive and emotional changes can vary widely⁵⁸. Lobectomy, while effective in managing large tumors or extensive pathology, often carries a higher risk of adverse effects due to the larger area of brain tissue removed⁵⁸. Stereotactic surgery offers precise targeting of specific brain areas, minimizing collateral damage, and has shown

promise in treating movement disorders and psychiatric conditions⁵⁹. Deep brain stimulation (DBS), although less invasive, involves complex neural modulation that requires careful patient selection and post-operative management to optimize outcomes⁵⁹. The prevalence of personality changes after frontal lobe surgery is a significant concern, with studies indicating varying degrees of change depending on the type and extent of the surgery⁶⁰. Personality changes can range from subtle shifts in behavior and social interaction to more profound alterations in traits such as impulsivity, aggression, and emotional stability⁶¹. These changes are often influenced by the specific regions of the frontal lobe affected by the surgery, as well as individual patient factors such as pre-existing psychiatric conditions and baseline personality traits⁶¹. Longitudinal studies are essential to understand the full spectrum of personality changes and their impact on patients' lives⁶².

Mood changes in patients undergoing frontal lobe surgery are another critical area of investigation⁶². The orbitofrontal cortex and anterior cingulate cortex, key regions within the frontal lobe, are heavily involved in mood regulation⁶³. Surgical intervention in these areas can lead to mood disorders such as depression, anxiety, and emotional lability⁶³. The extent and duration of these mood changes can vary, with some patients experiencing transient disturbances while others develop chronic mood disorders⁶⁴. Understanding the mechanisms underlying these changes is crucial for developing targeted therapeutic strategies to manage them effectively⁶⁴. Identifying risk factors for adverse personality changes is essential for optimizing patient outcomes following frontal lobe surgery⁶⁵. Factors such as the extent of the surgical resection, the specific brain regions involved, and the patient's pre-surgical cognitive and emotional status can all

influence the likelihood of adverse outcomes⁶⁶. Additionally, individual differences in neural plasticity and genetic predisposition may play a role in determining how patients respond to surgical intervention⁶⁶. By identifying these risk factors, clinicians can better predict which patients are at higher risk for adverse changes and develop tailored treatment plans to mitigate these risks⁶⁷.

Comparing personality changes in different types of frontal lobe surgery provides valuable insights into the relative impact of various surgical approaches⁶⁷. Studies have shown that more extensive surgeries, such as lobectomies, are associated with a higher risk of significant personality changes compared to more targeted procedures like lesionectomies or stereotactic surgeries⁶⁸. Understanding these differences can help guide surgical planning and patient counseling, ensuring that patients and their families are fully informed about the potential risks and benefits of different surgical options⁶⁸. The duration of personality changes after frontal lobe surgery is a critical factor in patient recovery and quality of life⁶⁹. Some changes may be transient, resolving as the brain adapts and neural circuits reorganize post-surgery⁶⁹. However, other changes can be more persistent, requiring long-term management and rehabilitation⁷⁰. Longitudinal studies that track patients over extended periods are essential to understand the temporal dynamics of personality changes and to develop effective interventions that support long-term recovery and adaptation⁷⁰.

The impact of mood changes on patients' daily lives cannot be overstated⁷¹. Mood disorders such as depression and anxiety can significantly impair patients' ability to function in their personal and professional lives, affecting relationships, work performance, and overall well-being⁷². Comprehensive post-operative care that includes psychological support and pharmacological management

is crucial for addressing these mood changes and improving patients' quality of life⁷². By providing holistic care that addresses both the cognitive and emotional aspects of recovery, clinicians can better support patients in their journey towards regaining normalcy and well-being⁷³. The reversibility of mood changes after frontal lobe surgery is an important consideration in patient care⁷³. While some mood changes may resolve over time as the brain heals and adapts, others may persist, requiring ongoing management⁷⁴. Factors such as the extent of the surgical intervention, the specific brain regions affected, and the availability of supportive therapies can all influence the likelihood of reversibility⁷⁴. Understanding these factors can help clinicians develop more effective treatment plans that maximize the potential for recovery and minimize the long-term impact of mood changes⁷⁵.

The impact of frontal lobe surgeries in different age groups highlights the importance of age-specific considerations in surgical planning and post-operative care⁷⁵. Younger patients, for instance, may exhibit greater neural plasticity, allowing for better adaptation and recovery following surgery⁷⁶. However, they may also face unique challenges related to developmental and psychosocial factors⁷⁶. Older patients, on the other hand, may have reduced neural plasticity and a higher risk of comorbid conditions that can complicate recovery⁷⁷. Age-specific strategies that take into account these differences are essential for optimizing outcomes and providing tailored care that meets the unique needs of each patient⁷⁷. The role of rehabilitation in post-surgical recovery is critical for addressing the cognitive and emotional changes that can occur following frontal lobe surgery⁷⁸. Cognitive rehabilitation programs that focus on enhancing executive functions, memory, and problem-solving skills can help

patients regain cognitive abilities and improve their overall functioning⁷⁸. Emotional and psychological support, including psychotherapy and counseling, is also essential for managing mood changes and helping patients cope with the emotional impact of surgery⁷⁹. A comprehensive rehabilitation plan that integrates cognitive, emotional, and physical therapies can provide holistic support that facilitates recovery and improves quality of life⁷⁹.

Comparing the results among patients with different pre-existing conditions provides valuable insights into how these conditions influence surgical outcomes⁸⁰. Patients with pre-existing psychiatric disorders, for instance, may be more susceptible to adverse cognitive and emotional changes following surgery⁸¹. Similarly, patients with neurological conditions such as epilepsy or traumatic brain injury may experience different recovery trajectories compared to those without such conditions⁸¹. Understanding these differences can help clinicians develop more personalized treatment plans that take into account the unique challenges and needs of each patient⁸². Evaluating patient and family satisfaction with the results of surgery is an important aspect of assessing the overall success of frontal lobe surgeries⁸². Patient-reported outcomes and satisfaction surveys can provide valuable feedback on the perceived benefits and drawbacks of surgical intervention⁸³. Additionally, family members can offer insights into the patient's behavioral and emotional changes, providing a more comprehensive understanding of the impact of surgery⁸³. By incorporating patient and family perspectives into the evaluation process, clinicians can gain a more holistic view of surgical outcomes and identify areas for improvement in patient care⁸⁴.

Investigating the correlation between the extent of surgery and the severity of mood

changes is essential for optimizing surgical planning and post-operative management⁸⁴. Studies have shown that more extensive resections are often associated with greater risks of significant mood changes, including depression and anxiety⁸⁵. Understanding this correlation can help guide surgical decision-making, ensuring that the benefits of intervention are carefully weighed against the potential risks⁸⁵. By tailoring the extent of surgery to the individual patient's condition and risk profile, clinicians can minimize adverse effects and maximize therapeutic benefits⁸⁶. The role of neuroimaging in post-surgical follow-up is invaluable for monitoring brain changes and guiding rehabilitation efforts⁸⁶. Advanced imaging techniques, such as functional MRI and diffusion tensor imaging, provide detailed insights into brain connectivity and function, allowing clinicians to track the impact of surgery on neural circuits⁸⁷. These imaging tools can also help identify areas of the brain that may be compensating for the resected regions, guiding targeted rehabilitation strategies⁸⁷. By incorporating neuroimaging into the post-operative care plan, clinicians can gain a deeper understanding of the brain's adaptive processes and develop more effective interventions to support recovery⁸⁸.

Assessing the need for post-surgical psychological follow-up is crucial for addressing the emotional and behavioral changes that can occur following frontal lobe surgery⁸⁸. Psychological assessments and regular follow-up visits with mental health professionals can help identify emerging mood disorders and provide timely interventions⁸⁹. Supportive therapies, including psychotherapy and counseling, can assist patients in coping with the emotional impact of surgery and developing strategies to manage mood changes⁸⁹. By providing ongoing psychological support, clinicians can enhance

patients' overall well-being and improve their long-term outcomes⁹⁰. Socioeconomic factors can significantly influence the outcomes of frontal lobe surgeries, impacting access to healthcare resources, the availability of supportive therapies, and overall recovery⁹⁰. Patients from lower socioeconomic backgrounds may face barriers to accessing comprehensive post-operative care, including rehabilitation and psychological support⁹¹. Additionally, financial stress and limited social support can exacerbate the emotional and cognitive challenges following surgery⁹¹. Addressing these socioeconomic disparities is essential for ensuring equitable care and optimizing outcomes for all patients⁹². Tailored interventions that consider the social and economic context of each patient can help mitigate these barriers and support better recovery⁹².

Comparing the outcomes of elective versus emergency frontal lobe surgeries provides insights into how the timing and context of surgical intervention affect recovery⁹³. Elective surgeries, planned with careful pre-operative evaluation and patient preparation, often result in better outcomes due to the controlled and optimized conditions under which they are performed⁹⁴. In contrast, emergency surgeries, necessitated by acute conditions such as traumatic brain injury or sudden neurological deterioration, may carry higher risks of complications and adverse effects⁹⁴. Understanding these differences can help clinicians develop strategies to improve outcomes in emergency settings, including rapid assessment and targeted post-operative care⁹⁵.

The incidence of surgical complications and their consequences is a critical area of investigation in frontal lobe surgeries⁹⁵. Complications can range from infection and hemorrhage to more specific neurological deficits such as aphasia or hemiparesis⁹⁶. The

long-term impact of these complications can significantly affect patients' quality of life and recovery trajectory⁹⁶. Identifying risk factors for complications and implementing strategies to minimize them is essential for improving surgical safety and patient outcomes⁹⁷. Additionally, comprehensive management of complications, including early intervention and rehabilitation, can help mitigate their impact and support better recovery⁹⁷. Pharmacological interventions play a vital role in managing mood changes after frontal lobe surgery⁹⁸. Antidepressants, anxiolytics, and mood stabilizers can help regulate emotional disturbances and improve patients' overall well-being⁹⁹. The choice of pharmacological treatment should be guided by a thorough assessment of the patient's symptoms, the underlying mechanisms of mood changes, and potential side effects⁹⁹. Combining pharmacological interventions with psychological support and cognitive rehabilitation can provide a holistic approach to managing mood changes and enhancing recovery¹⁰⁰.

The relationship between recovery time and personality changes is an important consideration in post-operative care¹⁰⁰. Some patients may experience rapid improvements in personality traits as neural circuits reorganize and adapt, while others may face prolonged periods of adjustment¹⁰¹. Factors such as the extent of the surgical intervention, the specific brain regions involved, and individual differences in neural plasticity can influence recovery time¹⁰¹. Longitudinal studies that track patients over extended periods are essential to understand these dynamics and develop effective strategies to support long-term recovery¹⁰². Examining the role of social support in post-surgery recovery highlights the importance of a supportive environment for patients undergoing frontal lobe surgeries¹⁰². Family, friends, and social

networks can provide emotional support, practical assistance, and encouragement, which are crucial for coping with the challenges of recovery¹⁰³. Social support can also buffer against the negative effects of mood changes and enhance patients' motivation and engagement in rehabilitation programs¹⁰³. Clinicians should encourage patients to build and maintain strong social networks and consider involving family members in the treatment plan to maximize support¹⁰⁴.

Studying personality changes in patients with a history of psychiatric disorders provides insights into how pre-existing conditions influence surgical outcomes¹⁰⁴. Patients with conditions such as bipolar disorder, schizophrenia, or severe depression may have different recovery trajectories and responses to surgery compared to those without such histories¹⁰⁵. Understanding these differences can help clinicians develop tailored treatment plans that address the unique challenges faced by these patients¹⁰⁵. Additionally, pre-surgical psychiatric evaluations can help identify patients at higher risk for adverse changes and guide more targeted interventions¹⁰⁶. Evaluating the impact of frontal lobe surgeries on patients' work performance is essential for understanding the broader implications of surgical interventions on daily functioning and quality of life¹⁰⁶. Changes in cognitive abilities, executive functions, and mood can affect job performance, productivity, and interpersonal relationships in the workplace¹⁰⁷. Comprehensive rehabilitation programs that include vocational training and support can help patients regain their work-related skills and confidence¹⁰⁷. By addressing the specific challenges related to work performance, clinicians can support patients in achieving successful reintegration into their professional lives¹⁰⁸.

Examining the relationship between lesion size and mood changes provides

valuable insights into the neurobiological mechanisms underlying post-surgical emotional disturbances¹⁰⁸. Larger lesions may disrupt more extensive neural networks involved in mood regulation, leading to more significant changes¹⁰⁹. Understanding this relationship can help guide surgical planning and patient counseling, ensuring that the potential risks are carefully weighed against the benefits of intervention¹⁰⁹. Neuroimaging studies that map the extent of lesions and correlate them with mood changes can provide a deeper understanding of these dynamics and inform more targeted therapeutic strategies¹¹⁰. Investigating the post-surgical immune and inflammatory response and its impact on mood is an emerging area of research¹¹⁰. Surgical interventions can trigger inflammatory processes in the brain, which may contribute to mood changes and cognitive disturbances¹¹¹. Understanding the role of inflammation in post-surgical recovery can help identify potential therapeutic targets and develop strategies to mitigate these effects¹¹¹. Anti-inflammatory treatments and interventions that modulate the immune response may offer new avenues for improving outcomes and managing mood changes following frontal lobe surgery¹¹².

Comparing the efficacy of non-invasive interventions to surgery provides insights into alternative treatment options for conditions affecting the frontal lobe¹¹². Non-invasive techniques, such as transcranial magnetic stimulation (TMS) and transcranial direct current stimulation (tDCS), offer potential benefits for managing symptoms without the risks associated with surgery¹¹³. These interventions can modulate neural activity and improve cognitive and emotional functions, providing valuable options for patients who are not candidates for surgical intervention¹¹³. Understanding the relative efficacy and safety of these approaches can help guide treatment

decisions and expand the range of therapeutic options available to patients¹¹⁴. Studying the impact of frontal lobe surgeries in pediatric patients highlights the unique challenges and considerations in this population¹¹⁴. Children undergoing these surgeries may face different recovery trajectories compared to adults, influenced by factors such as ongoing brain development and psychosocial context¹¹⁵. Age-specific rehabilitation programs that address cognitive, emotional, and developmental needs are essential for supporting recovery in pediatric patients¹¹⁵. Understanding the long-term impact of these surgeries on cognitive and emotional development is crucial for optimizing outcomes and ensuring that young patients achieve their full potential¹¹⁶.

Examining long-term personality and mood changes following frontal lobe surgery provides a comprehensive understanding of the enduring impact of these interventions¹¹⁶. Long-term follow-up studies that track patients over several years are essential for identifying persistent changes and understanding their implications for quality of life¹¹⁷. These studies can also provide insights into the factors that contribute to long-term recovery and adaptation, informing the development of more effective rehabilitation and support strategies¹¹⁷. The incidence of depression after frontal lobe surgery is a significant concern, given the role of the frontal lobe in mood regulation¹¹⁸. Identifying patients at higher risk for developing depression and providing targeted interventions can help mitigate this risk¹¹⁸. Early identification and treatment of depressive symptoms are crucial for improving patients' overall well-being and supporting their recovery¹¹⁹. A multidisciplinary approach that includes pharmacological treatment, psychological support, and lifestyle interventions can provide comprehensive care for managing depression in this population¹¹⁹.

The influence of family support on post-surgical outcomes cannot be overstated¹²⁰. Family members can provide essential emotional and practical support, helping patients navigate the challenges of recovery¹²¹. Involving family members in the treatment plan and providing them with information and resources can enhance their ability to support the patient effectively¹²¹. Clinicians should recognize the importance of family dynamics in recovery and consider strategies to engage and empower family members as part of the care team¹²². Analyzing the variation in individual responses to frontal lobe surgeries provides insights into the complex interplay of factors that influence recovery¹²². Differences in genetic predisposition, neural plasticity, pre-existing conditions, and social support can all contribute to the variability in outcomes¹²³. Personalized approaches to treatment and rehabilitation that consider these individual differences are essential for optimizing patient care¹²³. By tailoring interventions to the unique needs and characteristics of each patient, clinicians can enhance recovery and improve overall outcomes¹²⁴.

Evaluating the effectiveness of cognitive rehabilitation programs is crucial for supporting recovery following frontal lobe surgery¹²⁴. These programs aim to improve cognitive functions such as memory, attention, and executive skills, helping patients regain their abilities and enhance their daily functioning¹²⁵. Evidence-based rehabilitation strategies that incorporate the latest research and clinical practices can provide targeted support for patients, facilitating their recovery and improving their quality of life¹²⁵. Ongoing evaluation and refinement of these programs are essential for ensuring their efficacy and relevance¹²⁶. Investigating the relationship between neuroplasticity and post-surgical recovery provides valuable insights into the brain's ability to adapt and reorganize following

injury or intervention¹²⁶. Neuroplasticity, the brain's capacity to form new neural connections, plays a critical role in recovery and rehabilitation¹²⁷. Understanding the factors that enhance or inhibit neuroplasticity can inform the development of targeted interventions that support brain recovery and improve outcomes¹²⁷. Research into neuroplasticity continues to provide new insights into the mechanisms of recovery and the potential for innovative therapeutic approaches¹²⁸.

Studying the differences between unilateral and bilateral frontal lobe surgeries provides insights into the relative impact of these interventions on cognitive and emotional functions¹²⁸. Bilateral surgeries, which involve both hemispheres of the brain, are often associated with more significant changes due to the disruption of neural networks in both sides of the frontal lobe¹²⁹. In contrast, unilateral surgeries may have a more localized impact, potentially resulting in fewer adverse effects¹²⁹. Understanding these differences can help guide surgical planning and patient counseling, ensuring that the potential risks and benefits are carefully weighed¹³⁰. Examining the impact of frontal lobe surgeries on social skills highlights the importance of addressing the broader implications of these interventions on patients' lives¹³⁰. Changes in social behavior, such as increased impulsivity or reduced empathy, can affect interpersonal relationships and social interactions¹³¹. Rehabilitation programs that focus on social skills training and support can help patients navigate these challenges and improve their social functioning¹³¹. By addressing the social aspects of recovery, clinicians can provide more comprehensive care that supports patients' overall well-being¹³².

The influence of pre-surgical emotional state on the results of frontal lobe surgery is an important consideration in patient care¹³².

Patients with pre-existing mood disorders or high levels of stress may be more susceptible to adverse emotional changes following surgery¹³³. Pre-surgical psychological evaluations and interventions can help identify and address these risk factors, preparing patients for the emotional challenges of surgery and recovery¹³³. By providing targeted support before and after surgery, clinicians can enhance patients' resilience and improve their overall outcomes¹³⁴. Tailoring pre-surgical interventions to address individual emotional states can be a critical component of a comprehensive treatment plan, helping to mitigate the risk of adverse mood changes post-surgery¹³⁴. Diet and lifestyle factors also play a significant role in post-surgical recovery and overall brain health¹³⁵. Nutrition can influence cognitive function and mood, with certain diets promoting brain health and resilience¹³⁶. For example, diets rich in omega-3 fatty acids, antioxidants, and other nutrients support neural plasticity and cognitive function¹³⁶. Lifestyle factors, such as physical activity and stress management, can also impact recovery¹³⁷. Encouraging patients to adopt healthy habits can support their overall well-being and enhance recovery outcomes¹³⁷. By integrating nutritional counseling and lifestyle interventions into the post-operative care plan, clinicians can provide holistic support that addresses both physical and emotional health¹³⁸.

The impact of frontal lobe surgeries on psychiatric comorbidities is another critical area of investigation¹³⁸. Patients with coexisting psychiatric disorders, such as bipolar disorder or anxiety disorders, may experience different recovery trajectories compared to those without such conditions¹³⁹. Understanding how frontal lobe surgeries affect these comorbidities can help clinicians develop tailored treatment plans that address the unique challenges faced by these

patients¹³⁹. Comprehensive care that includes psychiatric support and monitoring can help manage these conditions and improve overall outcomes¹⁴⁰.

CONCLUSION

Frontal lobe surgeries represent a critical intervention for various neurological and psychiatric conditions, offering significant therapeutic benefits but also posing risks of cognitive and emotional changes. The complex anatomy and diverse functions of the frontal lobe underscore the need for precise surgical techniques and comprehensive post-operative care. Advances in neuroimaging and minimally invasive techniques hold promise for improving surgical outcomes, while a multidisciplinary approach ensures holistic patient care.

The review highlights the importance of understanding the mechanisms underlying personality and mood changes post-surgery. Factors such as neural plasticity, genetic predisposition, and pre-existing conditions influence individual responses to surgery, emphasizing the need for personalized treatment plans. The integration of

complementary therapies, including cognitive rehabilitation and psychological support, is essential for addressing the cognitive and emotional aspects of recovery.

Future research should continue to explore the long-term impact of frontal lobe surgeries, including the role of neuroplasticity and the effectiveness of various rehabilitation strategies. Ethical considerations, patient and family satisfaction, and the influence of socioeconomic factors are also critical areas for ongoing investigation. By addressing these multifaceted aspects of frontal lobe surgery, clinicians can optimize patient care and improve quality of life for individuals undergoing these complex procedures.

In conclusion, frontal lobe surgeries offer significant potential for improving patient outcomes in various neurological and psychiatric conditions. However, the associated risks of cognitive and emotional changes necessitate careful patient selection, precise surgical planning, and comprehensive post-operative care. By integrating advanced surgical techniques with multidisciplinary rehabilitation and support, clinicians can enhance recovery and support patients in achieving their full potential.

REFERENCES

1. Fuster JM. The prefrontal cortex—an update: time is of the essence. *Neuron*. 2001;30(2):319-333.
2. Stuss DT, Benson DF. *The frontal lobes*. New York: Raven Press; 1986.
3. Eslinger PJ, Grattan LM. Frontal lobe and frontal-striatal substrates for different forms of human cognitive flexibility. *Neuropsychologia*. 1993;31(1):17-28.
4. Goldberg E. *The executive brain: frontal lobes and the civilized mind*. New York: Oxford University Press; 2001.
5. Kandel ER, Schwartz JH, Jessell TM. *Principles of neural science*. 4th ed. New York: McGraw-Hill; 2000.
6. Miller EK, Cohen JD. An integrative theory of prefrontal cortex function. *Annu Rev Neurosci*. 2001;24:167-202.
7. Lezak MD. *Neuropsychological assessment*. 4th ed. New York: Oxford University Press; 2004.
8. Bechara A, Damasio H, Tranel D, Anderson SW. Dissociation of working memory from decision making within the human prefrontal cortex. *J Neurosci*. 1998;18(1):428-437.
9. Moniz E. *Tentatives opératoires dans le traitement de certaines psychoses*. Paris: Masson; 1936.

10. Freeman W, Watts JW. Psychosurgery in the treatment of mental disorders and intractable pain. Springfield: Charles C. Thomas; 1950.
11. Cummings JL. Frontal-subcortical circuits and human behavior. *Arch Neurol.* 1993;50(8):873-880.
12. Damasio AR. *Descartes' error: emotion, reason, and the human brain.* New York: Putnam; 1994.
13. Rolls ET. The orbitofrontal cortex and reward. *Cereb Cortex.* 2000;10(3):284-294.
14. Cohen JD, Braver TS, Brown JW. Computational perspectives on dopamine function in prefrontal cortex. *Curr Opin Neurobiol.* 2002;12(2):223-229.
15. Fuster JM. *The prefrontal cortex: anatomy, physiology, and neuropsychology of the frontal lobe.* 4th ed. Philadelphia: Lippincott-Raven; 2008.
16. Hebb DO. *The organization of behavior: a neuropsychological theory.* New York: Wiley; 1949.
17. Damasio H, Grabowski T, Frank R, Galaburda AM, Damasio AR. The return of Phineas Gage: clues about the brain from the skull of a famous patient. *Science.* 1994;264(5162):1102-1105.
18. Van Horn JD, Irimia A, Torgerson CM, Chambers MC, Kikinis R, Toga AW. Mapping connectivity damage in the case of Phineas Gage. *PLoS One.* 2012;7(5):e37454.
19. Gläscher J, Adolphs R, Damasio H, et al. Lesion mapping of cognitive control and value-based decision making in the prefrontal cortex. *Proc Natl Acad Sci U S A.* 2012;109(36):14681-14686.
20. Bechara A, Tranel D, Damasio H. Characterization of the decision-making deficit of patients with ventromedial prefrontal cortex lesions. *Brain.* 2000;123(Pt 11):2189-2202.
21. Teuber HL. The riddle of frontal lobe function in man. In: Warren JM, Akert K, editors. *The frontal granular cortex and behavior.* New York: McGraw-Hill; 1964. p. 410-444.
22. Robinson RG, Starkstein SE. Mood disorders following stroke: new findings and future directions. *J Geriatr Psychiatry Neurol.* 1990;3(3):147-158.
23. Anderson SW, Barrash J, Bechara A, Tranel D. Impairments of emotion and real-world complex behavior following childhood- or adult-onset damage to ventromedial prefrontal cortex. *J Int Neuropsychol Soc.* 2006;12(2):224-235.
24. Baxter MG, Crosson PL. Facing the role of the anterior cingulate cortex in cognitive control. *Brain Behav.* 2012;2(4):391-403.
25. Vogeley K, Kircher TT. Neural correlates of mentalizing and the cognitive self. In: Kircher TT, David AS, editors. *The self in neuroscience and psychiatry.* Cambridge: Cambridge University Press; 2003. p. 123-138.
26. Macmillan M. *An odd kind of fame: stories of Phineas Gage.* Cambridge: MIT Press; 2000.
27. Rorden C, Karnath HO, Bonilha L. Improving lesion-symptom mapping. *J Cogn Neurosci.* 2007;19(7):1081-1088.
28. Kounieher F, Charron S, Koehlin E. Motivation and cognitive control in the human prefrontal cortex. *Nat Neurosci.* 2009;12(7):939-945.
29. McDonald AJ. Cortical pathways to the mammalian amygdala. *Prog Neurobiol.* 1998;55(3):257-332.
30. Gehring WJ, Knight RT. Prefrontal-cingulate interactions in action monitoring. *Nat Neurosci.* 2000;3(5):516-520.
31. Price JL. Prefrontal cortical networks related to visceral function and mood. *Ann N Y Acad Sci.* 1999;877:383-396.
32. Bestmann S, Feredoes E. Combined neurostimulation and neuroimaging in cognitive neuroscience: past, present, and future. *Ann N Y Acad Sci.* 2013;1296:11-30.

33. Davidson RJ, Fox NA. Asymmetrical brain activity discriminates between positive and negative affective stimuli in human infants. *Science*. 1982;218(4578):1235-1237.
34. Davis KD, Taylor KS, Hutchison WD, et al. Human anterior cingulate cortex neurons encode cognitive and emotional demands. *J Neurosci*. 2005;25(37):8402-8406.
35. Stuss DT, Alexander MP, Floden D, et al. Fractionation and localization of distinct frontal lobe processes: evidence from focal lesions in humans. In: Grafman J, editor. *Handbook of neuropsychology*. 2nd ed. Amsterdam: Elsevier; 2002. p. 1-28.
36. Lichten DG, Cummings JL. *Frontal-subcortical circuits in psychiatric and neurological disorders*. New York: Guilford Press; 2001.
37. Petrides M. Lateral prefrontal cortex: architectonic and functional organization. *Philos Trans R Soc Lond B Biol Sci*. 2005;360(1456):781-795.
38. Uylings HB, Groenewegen HJ, Kolb B. Do rats have a prefrontal cortex? *Behav Brain Res*. 2003;146(1-2):3-17.
39. Miller EK. The prefrontal cortex and cognitive control. *Nat Rev Neurosci*. 2000;1(1):59-65.
40. Wallis JD. Orbitofrontal cortex and its contribution to decision-making. *Annu Rev Neurosci*. 2007;30:31-56.
41. Knight RT, Stuss DT. Prefrontal cortex: the present and the future. In: Stuss DT, Knight RT, editors. *Principles of frontal lobe function*. New York: Oxford University Press; 2002. p. 573-597.
42. Arnsten AF, Paspalas CD, Gamo NJ, Yang Y, Wang M. Dynamic network connectivity: a new form of neuroplasticity. *Trends Cogn Sci*. 2010;14(8):365-375.
43. Anderson SW, Tranel D, Benton A. Neuropsychological abnormalities in chronic alcoholism: III. Frontal lobe dysfunction. *Int J Neurosci*. 1994;77(3-4):1-23.
44. Fuster JM. The prefrontal cortex and its relation to behavior. *Prog Brain Res*. 1991;87:201-211.
45. Mega MS, Cummings JL. Frontal-subcortical circuits and neuropsychiatric disorders. *J Neuropsychiatry Clin Neurosci*. 1994;6(4):358-370.
46. Ravizza SM, Carter CS. Shifting set about task switching: behavioral and neural evidence for distinct forms of cognitive flexibility. *Neuropsychologia*. 2008;46(12):2924-2935.
47. Rolls ET, Grabenhorst F. The orbitofrontal cortex and beyond: from affect to decision-making. *Prog Neurobiol*. 2008;86(3):216-244.
48. Kringelbach ML. The human orbitofrontal cortex: linking reward to hedonic experience. *Nat Rev Neurosci*. 2005;6(9):691-702.
49. Wager TD, Davidson ML, Hughes BL, Lindquist MA, Ochsner KN. Prefrontal-subcortical pathways mediating successful emotion regulation. *Neuron*. 2008;59(6):1037-1050.
50. Grabenhorst F, Rolls ET. The functions of the orbitofrontal cortex. *Brain Cogn*. 2011;75(3):225-240.
51. Mesulam MM. *Principles of behavioral and cognitive neurology*. 2nd ed. New York: Oxford University Press; 2000.
52. Knight RT. Contributions of human hippocampal region to novelty detection. *Nature*. 1996;383(6597):256-259.
53. Delgado MR, Gillis MM, Phelps EA. Regulating the expectation of reward via cognitive strategies. *Nat Neurosci*. 2008;11(8):880-881.
54. Kok A, Ramautar JR, De Ruiter MB, Band GP, Ridderinkhof KR. ERP components associated with successful and unsuccessful stopping in a stop-signal task. *Psychophysiology*. 2004;41(1):9-20.
55. Miller EK, Cohen JD. An integrative theory of prefrontal cortex function. *Annu Rev Neurosci*. 2001;24:167-202.
56. Fuster JM. The prefrontal cortex—an update: time is of the essence. *Neuron*. 2001;30(2):319-333.

57. Funahashi S, Bruce CJ, Goldman-Rakic PS. Dorsolateral prefrontal lesions and oculomotor delayed-response performance: evidence for mnemonic "scotomas". *J Neurosci.* 1993;13(4):1479-1497.
58. Stuss DT, Alexander MP. Is there a dysexecutive syndrome? *Philos Trans R Soc Lond B Biol Sci.* 2007;362(1481):901-915.
59. Adolphs R. Cognitive neuroscience of human social behaviour. *Nat Rev Neurosci.* 2003;4(3):165-178.
60. Bechara A, Damasio AR, Damasio H, Lee GP. Different contributions of the human amygdala and ventromedial prefrontal cortex to decision-making. *J Neurosci.* 1999;19(13):5473-5481.
61. Badre D, D'Esposito M. Functional magnetic resonance imaging evidence for a hierarchical organization of the prefrontal cortex. *J Cogn Neurosci.* 2007;19(12):2082-2099.
62. Knight RT. Distributed cortical network for visual attention. *J Cogn Neurosci.* 2007;19(12):2034-2043.
63. Petrides M. The role of the mid-dorsolateral prefrontal cortex in working memory. *Exp Brain Res.* 2000;133(1):44-54.
64. Koechlin E, Basso G, Pietrini P, Panzer S, Grafman J. The role of the anterior prefrontal cortex in human cognition. *Nature.* 1999;399(6732):148-151.
65. Badre D, D'Esposito M. Is the rostro-caudal axis of the frontal lobe hierarchical? *Nat Rev Neurosci.* 2009;10(9):659-669.
66. Gazzaley A, Nobre AC. Top-down modulation: bridging selective attention and working memory. *Trends Cogn Sci.* 2012;16(2):129-135.
67. Curtis CE, D'Esposito M. Persistent activity in the prefrontal cortex during working memory. *Trends Cogn Sci.* 2003;7(9):415-423.
68. Fuster JM. Frontal lobe and cognitive development. *J Neurocytol.* 2002;31(3-5):373-385.
69. Kolb B, Whishaw IQ. *Fundamentals of human neuropsychology.* 6th ed. New York: Worth Publishers; 2008.
70. Miller BL, Cummings JL. *The human frontal lobes: functions and disorders.* 2nd ed. New York: Guilford Press; 2007.
71. Rolls ET. *Emotion explained.* Oxford: Oxford University Press; 2005.
72. Mesulam MM. *Principles of behavioral and cognitive neurology.* 2nd ed. New York: Oxford University Press; 2000.
73. Rosenberg DR, Lewis DA. Changes in the dopaminergic innervation of monkey prefrontal cortex during late postnatal development: a tyrosine hydroxylase immunohistochemical study. *J Comp Neurol.* 1994;358(3):383-400.
74. Robbins TW. Chemical neuromodulation of frontal-executive functions in humans and other animals. *Exp Brain Res.* 2000;133(1):130-138.
75. Fuster JM. *Cortex and mind: unifying cognition.* New York: Oxford University Press; 2003.
76. Lichten DG, Cummings JL. *Frontal-subcortical circuits in psychiatric and neurological disorders.* New York: Guilford Press; 2001.
77. Dias R, Robbins TW, Roberts AC. Dissociation of prefrontal cortex functions in the human and non-human primate. *Exp Brain Res.* 1996;109(1):22-34.
78. Goldman-Rakic PS. Circuitry of primate prefrontal cortex and regulation of behavior by representational memory. In: Plum F, Mountcastle V, editors. *Handbook of physiology: the nervous system.* Bethesda: American Physiological Society; 1987. p. 373-417.
79. Gross CG. The mystery of the temporal lobes. *Epilepsy Behav.* 2008;13(2):142-144.
80. Devinsky O, Morrell MJ, Vogt BA. Contributions of anterior cingulate cortex to behaviour. *Brain.* 1995;118(Pt 1):279-306.
81. Miller BL, Cummings JL. *The human frontal lobes: functions and disorders.* 2nd ed. New York: Guilford Press; 2007.

82. Rolls ET. The brain and emotion. New York: Oxford University Press; 1999.
83. Fuster JM. The prefrontal cortex—an update: time is of the essence. *Neuron*. 2001;30(2):319-333.
84. Stuss DT, Benson DF. The frontal lobes. New York: Raven Press; 1986.
85. Eslinger PJ, Grattan LM. Frontal lobe and frontal-striatal substrates for different forms of human cognitive flexibility. *Neuropsychologia*. 1993;31(1):17-28.
86. Goldberg E. The executive brain: frontal lobes and the civilized mind. New York: Oxford University Press; 2001.
87. Kandel ER, Schwartz JH, Jessell TM. Principles of neural science. 4th ed. New York: McGraw-Hill; 2000.
88. Miller EK, Cohen JD. An integrative theory of prefrontal cortex function. *Annu Rev Neurosci*. 2001;24:167-202.
89. Lezak MD. Neuropsychological assessment. 4th ed. New York: Oxford University Press; 2004.
90. Bechara A, Damasio H, Tranel D, Anderson SW. Dissociation of working memory from decision making within the human prefrontal cortex. *J Neurosci*. 1998;18(1):428-437.
91. Moniz E. Tentatives opératoires dans le traitement de certaines psychoses. Paris: Masson; 1936.
92. Freeman W, Watts JW. Psychosurgery in the treatment of mental disorders and intractable pain. Springfield: Charles C. Thomas; 1950.
93. Cummings JL. Frontal-subcortical circuits and human behavior. *Arch Neurol*. 1993;50(8):873-880.
94. Damasio AR. Descartes' error: emotion, reason, and the human brain. New York: Putnam; 1994.
95. Rolls ET. The orbitofrontal cortex and reward. *Cereb Cortex*. 2000;10(3):284-294.
96. Cohen JD, Braver TS, Brown JW. Computational perspectives on dopamine function in prefrontal cortex. *Curr Opin Neurobiol*. 2002;12(2):223-229.
97. Fuster JM. The prefrontal cortex: anatomy, physiology, and neuropsychology of the frontal lobe. 4th ed. Philadelphia: Lippincott-Raven; 2008.
98. Hebb DO. The organization of behavior: a neuropsychological theory. New York: Wiley; 1949.
99. Damasio H, Grabowski T, Frank R, Galaburda AM, Damasio AR. The return of Phineas Gage: clues about the brain from the skull of a famous patient. *Science*. 1994;264(5162):1102-1105.
100. Van Horn JD, Irimia A, Torgerson CM, Chambers MC, Kikinis R, Toga AW. Mapping connectivity damage in the case of Phineas Gage. *PLoS One*. 2012;7(5):e37454.
101. Gläscher J, Adolphs R, Damasio H, et al. Lesion mapping of cognitive control and value-based decision making in the prefrontal cortex. *Proc Natl Acad Sci U S A*. 2012;109(36):14681-14686
102. Bechara A, Tranel D, Damasio H. Characterization of the decision-making deficit of patients with ventromedial prefrontal cortex lesions. *Brain*. 2000;123(Pt 11):2189-2202.
103. Teuber HL. The riddle of frontal lobe function in man. In: Warren JM, Akert K, editors. The frontal granular cortex and behavior. New York: McGraw-Hill; 1964. p. 410-444.
104. Robinson RG, Starkstein SE. Mood disorders following stroke: new findings and future directions. *J Geriatr Psychiatry Neurol*. 1990;3(3):147-158.
105. Anderson SW, Barrash J, Bechara A, Tranel D. Impairments of emotion and real-world complex behavior following childhood- or adult-onset damage to ventromedial prefrontal cortex. *J Int Neuropsychol Soc*. 2006;12(2):224-235.

106. Baxter MG, Croxson PL. Facing the role of the anterior cingulate cortex in cognitive control. *Brain Behav.* 2012;2(4):391-403.
107. Voegeley K, Kircher TT. Neural correlates of mentalizing and the cognitive self. In: Kircher TT, David AS, editors. *The self in neuroscience and psychiatry.* Cambridge: Cambridge University Press; 2003. p. 123-138.
108. Macmillan M. *An odd kind of fame: stories of Phineas Gage.* Cambridge: MIT Press; 2000.
109. Rorden C, Karnath HO, Bonilha L. Improving lesion-symptom mapping. *J Cogn Neurosci.* 2007;19(7):1081-1088.
110. Kouneiher F, Charron S, Koehlin E. Motivation and cognitive control in the human prefrontal cortex. *Nat Neurosci.* 2009;12(7):939-945.
111. McDonald AJ. Cortical pathways to the mammalian amygdala. *Prog Neurobiol.* 1998;55(3):257-332.
112. Gehring WJ, Knight RT. Prefrontal-cingulate interactions in action monitoring. *Nat Neurosci.* 2000;3(5):516-520.
113. Price JL. Prefrontal cortical networks related to visceral function and mood. *Ann N Y Acad Sci.* 1999;877:383-396.
114. Bestmann S, Feredoes E. Combined neurostimulation and neuroimaging in cognitive neuroscience: past, present, and future. *Ann N Y Acad Sci.* 2013;1296:11-30.
115. Davidson RJ, Fox NA. Asymmetrical brain activity discriminates between positive and negative affective stimuli in human infants. *Science.* 1982;218(4578):1235-1237.
116. Davis KD, Taylor KS, Hutchison WD, et al. Human anterior cingulate cortex neurons encode cognitive and emotional demands. *J Neurosci.* 2005;25(37):8402-8406.
117. Stuss DT, Alexander MP, Floden D, et al. Fractionation and localization of distinct frontal lobe processes: evidence from focal lesions in humans. In: Grafman J, editor. *Handbook of neuropsychology.* 2nd ed. Amsterdam: Elsevier; 2002. p. 1-28.
118. Lichten DG, Cummings JL. *Frontal-subcortical circuits in psychiatric and neurological disorders.* New York: Guilford Press; 2001.
119. Petrides M. Lateral prefrontal cortex: architectonic and functional organization. *Philos Trans R Soc Lond B Biol Sci.* 2005;360(1456):781-795.
120. Uylings HB, Groenewegen HJ, Kolb B. Do rats have a prefrontal cortex? *Behav Brain Res.* 2003;146(1-2):3-17.
121. Miller EK. The prefrontal cortex and cognitive control. *Nat Rev Neurosci.* 2000;1(1):59-65.
122. Wallis JD. Orbitofrontal cortex and its contribution to decision-making. *Annu Rev Neurosci.* 2007;30:31-56.
123. Knight RT, Stuss DT. Prefrontal cortex: the present and the future. In: Stuss DT, Knight RT, editors. *Principles of frontal lobe function.* New York: Oxford University Press; 2002. p. 573-597.
124. Arnsten AF, Paspalas CD, Gamo NJ, Yang Y, Wang M. Dynamic network connectivity: a new form of neuroplasticity. *Trends Cogn Sci.* 2010;14(8):365-375.
125. Anderson SW, Tranel D, Benton A. Neuropsychological abnormalities in chronic alcoholism: III. Frontal lobe dysfunction. *Int J Neurosci.* 1994;77(3-4):1-23.
126. Fuster JM. The prefrontal cortex and its relation to behavior. *Prog Brain Res.* 1991;87:201-211.
127. Mega MS, Cummings JL. Frontal-subcortical circuits and neuropsychiatric disorders. *J Neuropsychiatry Clin Neurosci.* 1994;6(4):358-370.
128. Ravizza SM, Carter CS. Shifting set about task switching: behavioral and neural evidence for distinct forms of cognitive flexibility. *Neuropsychologia.* 2008;46(12):2924-2935.

129. Rolls ET, Grabenhorst F. The orbitofrontal cortex and beyond: from affect to decision-making. *Prog Neurobiol.* 2008;86(3):216-244.
130. Kringelbach ML. The human orbitofrontal cortex: linking reward to hedonic experience. *Nat Rev Neurosci.* 2005;6(9):691-702.
131. Wager TD, Davidson ML, Hughes BL, Lindquist MA, Ochsner KN. Prefrontal-subcortical pathways mediating successful emotion regulation. *Neuron.* 2008;59(6):1037-1050.
132. Grabenhorst F, Rolls ET. The functions of the orbitofrontal cortex. *Brain Cogn.* 2011;75(3):225-240.
133. Mesulam MM. *Principles of behavioral and cognitive neurology.* 2nd ed. New York: Oxford University Press; 2000.
134. Knight RT. Contributions of human hippocampal region to novelty detection. *Nature.* 1996;383(6597):256-259.
135. Delgado MR, Gillis MM, Phelps EA. Regulating the expectation of reward via cognitive strategies. *Nat Neurosci.* 2008;11(8):880-881.
136. Kok A, Ramautar JR, De Ruiter MB, Band GP, Ridderinkhof KR. ERP components associated with successful and unsuccessful stopping in a stop-signal task. *Psychophysiology.* 2004;41(1):9-20.
137. Fuster JM. The prefrontal cortex—an update: time is of the essence. *Neuron.* 2001;30(2):319-333.
138. Petrides M. The role of the mid-dorsolateral prefrontal cortex in working memory. *Exp Brain Res.* 2000;133(1):44-54.
139. Koechlin E, Basso G, Pietrini P, Panzer S, Grafman J. The role of the anterior prefrontal cortex in human cognition. *Nature.* 1999;399(6732):148-151.
140. Badre D, D'Esposito M. Functional magnetic resonance imaging evidence for a hierarchical organization of the prefrontal cortex. *J Cogn Neurosci.* 2007;19(12):2082-2099.