All Sciences Academy

CONTEMPORARY RESEARCH IN HEALTH SCIENCES

CONTEMPORARY RESEARCH IN HEALTH SCIENCES

Editor
Prof. Dr. Fatih HATİPOĞLU

Contemporary Research in Health Sciences
Editor: Prof. Dr. Fatih HATİPOĞLU

Design: All Sciences Academy Design
Published Date: August 2025
Publisher's Certification Number: 72273
ISBN: 978-625-5794-05-5

© All Sciences Academy

www.allsciencesacademy.com
allsciencesacademy@gmail.com

CONTENT

The Dual-Path Model of Emotional Intelligence: A New Perspective on Positive and Negative Pathways

Dr. Hina ZAHOOR

Assistant Professor, Istanbul Gelisim University, Faculty of Health Sciences

ABSTRACT

This paper presents the Dual-Path model of Emotional Intelligence (EI), which proposes two distinct forms of emotional intelligence: Positive Emotional Intelligence (PEI) and Negative Emotional Intelligence (NEI). The Dual-Path model of Emotional Intelligence (EI) offers a nuanced framework that highlights both the constructive and destructive potentials of emotional competencies. This model categorizes EI into two distinct pathways: Positive Emotional Intelligence (PEI) and Negative Emotional Intelligence (NEI). The PEI path emphasizes ethical applications of EI, including empathy, motivation, self-regulation, and ethical behavior, which foster positive social and organizational outcomes. Conversely, the NEI path sheds light on the misuse of emotional intelligence through manipulation, deception, and unethical behavior, leading to detrimental effects in social and workplace environments. This dual-path framework challenges the conventional view of EI as inherently positive, stressing that the same emotional skills can be directed toward harmful ends. Recognizing both the bright and dark sides of EI is critical for leadership, team dynamics, and organizational ethics. The model underscores the need for awareness, training, and ethical oversight in developing and applying emotional intelligence in professional settings. It invites further research into the predictors, contexts, and consequences of both PEI and NEI to inform leadership development, psychological assessment, and ethical interventions in organizational behavior. By acknowledging the dual nature of EI, this model provides a more comprehensive understanding of how emotional intelligence operates in diverse interpersonal and institutional contexts.

Keywords-Emotional Intelligence, Positive EI, Negative EI, Ethical Behavior, Organizational Outcomes.

INTRODUCTION

Emotional Intelligence (EI), often referred to as Emotional Quotient (EQ), has emerged as a pivotal factor in determining success across personal and professional domains. Defined as the capacity to perceive, interpret, manage, and harness emotions effectively, EI influences how individuals navigate social complexities, make decisions, and achieve positive outcomes (Goleman, 1995). In personal contexts, high EI fosters enhanced relationships, improved communication, and greater emotional well-being. Professionally, it contributes to effective leadership, teamwork, and conflict resolution, thereby promoting a productive work environment (University Canada West, 2023).

Despite the extensive research underscoring the benefits of EI, existing literature predominantly emphasizes its positive aspects, often overlooking the potential for its manipulative application. This oversight presents a significant gap in understanding the dual nature of EI. While EI can be employed to foster empathy and collaboration, it can also be utilized unethically to manipulate and exploit others for personal gain. Recognizing this dichotomy is crucial for a comprehensive understanding of EI's role in social interactions.

Addressing this gap, the present paper introduces the Dual-Path model of Emotional Intelligence, delineating two distinct pathways: Positive Emotional Intelligence (PEI) and Negative Emotional Intelligence (NEI). PEI encompasses the ethical and empathetic use of emotional awareness to build trust and enhance collective well-being. Conversely, NEI involves the manipulative use of emotional understanding to deceive or control others for self-serving purposes. This bifurcation offers a nuanced perspective on EI, acknowledging its potential to both strengthen and undermine social bonds.

The purpose of this paper is to elaborate on the Dual-Path model, exploring the characteristics, motivations, and social implications of PEI and NEI. By integrating insights from emotional regulation theories and self-determination theory, the paper aims to provide a comprehensive framework for understanding how the ethical or unethical application of EI influences interpersonal relationships and social dynamics. This exploration is significant as it not only broadens the conceptualization of EI but also informs interventions aimed at promoting ethical emotional practices in various settings, including leadership, healthcare, education, and organizational development.

In conclusion, while EI is widely recognized for its positive contributions to personal and professional success, acknowledging its dual potential is essential. The Dual-Path model offers a critical lens through which to examine the ethical dimensions of EI, emphasizing the importance of fostering PEI to cultivate harmonious social interactions and mitigate the risks associated with NEI.

THEORETICAL BACKGROUND OF EMOTIONAL INTELLIGENCE

Evolution of Emotional Intelligence

The concept of Emotional Intelligence (EI) has evolved significantly since its inception, drawing from various psychological theories and models. The term "emotional intelligence" was first introduced by Salovey and Mayer in 1990,

defining it as "the ability to monitor one's own and others' feelings and emotions, to discriminate among them and to use this information to guide one's thinking and actions" (Mayer & Salovey, 1990). Their model emphasized the role of emotions in enhancing cognitive processes and decision-making.

Building upon this foundation, Daniel Goleman popularized the concept in his 1995 book "Emotional Intelligence: Why It Can Matter More Than IQ," where he expanded the definition to include a set of skills and competencies that influence leadership, performance, and interpersonal effectiveness (Goleman, 1995). Goleman's model comprises five key components: self-awareness, self-regulation, motivation, empathy, and social skills.

Reuven Bar-On contributed to the field by developing the Emotional Quotient Inventory (EQ-i), a self-report measure designed to assess a range of emotional and social competencies (Bar-On, 1997). His model focuses on the ability to understand and manage emotions, cope with stress, and maintain interpersonal relationships.

The evolution of EI reflects a growing recognition of the importance of emotional and social competencies in personal and professional success. These foundational models have paved the way for extensive research into the applications and implications of EI across various domains.

Table 1: Evolution of Emotional Intelligence — Key Theories and Definitions

Researcher(s)	**Key Contributions**	**Year**
Salovey & Mayer	Defined EI as the ability to perceive, understand, and regulate emotions	1990
Goleman	Popularized EI, emphasizing its role in leadership and social success	1995
Bar-On	Developed an EI model focusing on emotional-social intelligence	1997
Mayer–Salovey–Caruso	Introduced ability model of EI focusing on emotional reasoning	2004

Emotional Intelligence in Social Contexts

Emotional intelligence plays a crucial role in shaping interpersonal relationships and social dynamics. Individuals with high EI are better equipped to navigate social complexities, communicate effectively, and build strong, empathetic connections with others.

Research has demonstrated a positive correlation between EI and various aspects of social functioning. For instance, Lopes et al. (2004) found that individuals with higher emotional intelligence exhibited greater social competence, including better conflict resolution skills and more positive interactions with peers. Similarly, Schutte et al. (2001) reported that higher EI was associated with increased empathy, prosocial behavior, and relationship satisfaction.

In organizational settings, EI has been linked to improved teamwork, leadership effectiveness, and job performance. A meta-analysis by O'Boyle et al. (2011) revealed that emotional intelligence is a significant predictor of job performance across various industries and roles. Moreover, EI contributes to enhanced communication, reduced workplace stress, and increased employee engagement (Cherniss, 2010).

These findings underscore the importance of emotional intelligence in fostering positive social interactions and creating supportive, collaborative environments.

Ethical and Manipulative Dimensions of Emotional Intelligence

While emotional intelligence is often associated with positive outcomes, it is essential to acknowledge its potential for manipulative or unethical use. The same skills that enable individuals to understand and influence emotions can be employed to deceive, manipulate, or exploit others for personal gain.

Salovey and Mayer (1990) acknowledged this duality, noting that emotional skills could be used for both prosocial and antisocial purposes. Subsequent research has explored the "dark side" of EI, examining how individuals may leverage emotional competencies unethically. For example, Austin et al. (2007) found that individuals with high EI and Machiavellian traits were more likely to engage in emotional manipulation. Similarly, Côté et al. (2011) reported that individuals with high EI could use their skills to achieve personal goals at the expense of others, particularly when driven by self-serving motivations.

These studies highlight the importance of considering the ethical implications of emotional intelligence. Developing EI should involve not only enhancing emotional competencies but also fostering ethical awareness and empathy to ensure that these skills are applied constructively.

THE DUAL-PATH MODEL OF EMOTIONAL INTELLIGENCE

Conceptual Overview

The Dual-Path model of Emotional Intelligence (EI) posits that EI manifests in two distinct forms: Positive Emotional Intelligence (PEI) and Negative Emotional Intelligence (NEI). While both involve the capacity to perceive, understand, and manage emotions, they diverge in their application and impact on interpersonal relationships.

Positive Emotional Intelligence (PEI) refers to the ethical and empathetic use of emotional awareness to foster trust, collaboration, and collective well-being. Individuals exhibiting PEI utilize their emotional skills to enhance social harmony and support others constructively.

In contrast, **Negative Emotional Intelligence (NEI)** involves the manipulative use of emotional awareness for personal gain, often at the expense of others. NEI is characterized by the strategic exploitation of emotions to deceive, control, or dominate, leading to conflict and mistrust in social interactions.

This bifurcation underscores the dual nature of EI, highlighting that the same emotional competencies can lead to vastly different outcomes depending on the individual's motivations and ethical considerations.

Core Constructs and Mechanisms

Both PEI and NEI encompass five core components: self-awareness, self-regulation, empathy, social skills, and motivation. However, the expression and utilization of these components differ markedly between the two forms.

- **Self-Awareness**: In PEI, self-awareness involves recognizing one's emotions and understanding their impact on behavior, facilitating personal growth and ethical decision-making. Conversely, in NEI, self-awareness may be used to mask true intentions and manipulate others' perceptions for self-serving purposes.
- **Self-Regulation**: PEI entails managing emotions to respond appropriately to situations, maintaining composure, and demonstrating integrity. NEI, however, may involve suppressing emotions to feign sincerity or exploit situations, often leading to deceptive behavior.
- **Empathy**: Empathy in PEI is characterized by genuine concern for others, enabling supportive and compassionate interactions. In NEI, empathy may be superficial, used to identify and exploit others' vulnerabilities for personal advantage.

- **Social Skills**: Individuals with PEI employ social skills to build meaningful relationships, resolve conflicts, and foster teamwork. Those with NEI may use these skills to manipulate social situations, spread misinformation, or undermine others.
- **Motivation**: PEI is driven by intrinsic motivation, focusing on personal development and contributing to the greater good. NEI is often fueled by extrinsic motivation, seeking power, recognition, or material gain, regardless of ethical implications.

Understanding these mechanisms is crucial for distinguishing between constructive and destructive applications of EI.

Emotional Vibes and Social Impact

The application of PEI and NEI significantly influences the emotional atmosphere, or "vibes," within social interactions, thereby affecting interpersonal dynamics.

Positive Emotional Intelligence fosters positive vibes, creating environments characterized by trust, openness, and mutual respect. These vibes enhance collaboration, reduce conflicts, and promote psychological safety, leading to stronger, more resilient relationships.

For instance, in organizational settings, leaders exhibiting PEI can inspire and motivate teams, leading to increased productivity and job satisfaction. Their ability to manage emotions and empathize with employees cultivates a supportive work culture, encouraging innovation and adaptability.

Negative Emotional Intelligence, on the other hand, generates negative vibes, resulting in tension, suspicion, and emotional distress. Such environments are prone to conflicts, reduced cooperation, and high turnover rates. Individuals employing NEI may achieve short-term objectives through manipulation, but often at the cost of long-term relationships and reputational damage.

In personal relationships, NEI can lead to emotional abuse, erosion of trust, and psychological harm. Recognizing and addressing NEI behaviors is essential for maintaining healthy interpersonal connections and fostering emotional well-being.

Table 2: Comparison of Positive Emotional Intelligence (PEI) vs Negative Emotional Intelligence (NEI)

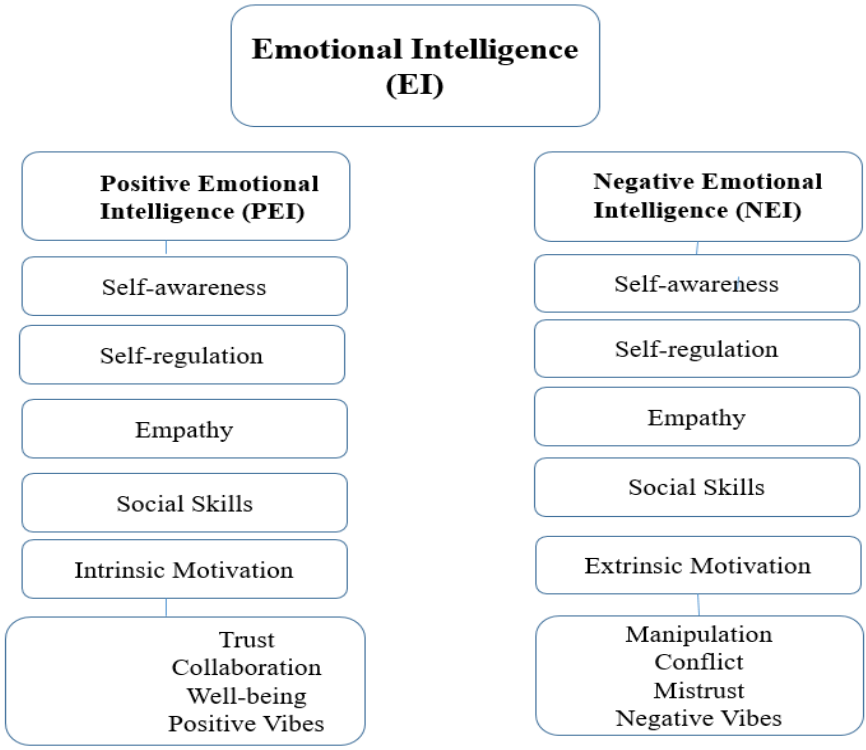
Component	**PEI**	**NEI**
Self-awareness	Recognizing emotions for personal growth and empathy	Recognizing emotions to mask true intentions
Self-regulation	Managing emotions constructively	Controlling emotions strategically for manipulation
Empathy	Understanding others' feelings to support and connect	Using empathy to exploit others
Social skills	Promoting cooperation and trust	Influencing or dominating others
Motivation	Intrinsic, growth-oriented	Extrinsic, self-serving

The Dual-Path model of Emotional Intelligence provides a comprehensive framework for understanding the divergent applications of EI. By distinguishing between PEI and NEI, individuals and organizations can better assess emotional competencies, promote ethical behavior, and mitigate the adverse effects of manipulative emotional practices. Cultivating PEI is imperative for building constructive relationships, enhancing social cohesion, and achieving sustainable success across various domains.

CONCEPTUAL MODEL DEVELOPMENT

Model Illustration

The Dual-Path model of Emotional Intelligence (EI) conceptualizes two distinct pathways through which individuals apply their emotional competencies: Positive Emotional Intelligence (PEI) and Negative Emotional Intelligence (NEI). These pathways are differentiated by the individual's motivations and the ethical application of emotional skills.



Source(Author)

This model illustrates how the same emotional competencies can lead to divergent social outcomes based on the individual's underlying motivations and ethical considerations.

Theoretical Justification

The Dual-Path Model integrates several psychological theories to substantiate its components and pathways:

- **Emotional Regulation Theory:** Gross (1998) posits that emotional regulation involves the processes by which individuals influence their emotions, how they experience them, and how they express them. In the context of PEI, individuals utilize emotional regulation to manage their emotions constructively, fostering positive social interactions. Conversely, in NEI, individuals may regulate their emotions strategically to manipulate others, leading to adverse social outcomes.
- **Self-Determination Theory (SDT):** Deci and Ryan (1985) emphasize the role of intrinsic and extrinsic motivations in human behavior. PEI aligns with intrinsic motivation, where actions are driven by internal satisfaction and ethical considerations. NEI

corresponds with extrinsic motivation, where behaviors are influenced by external rewards or pressures, potentially leading to manipulative practices.

- **Social Exchange Theory:** Homans (1958) suggests that social behavior is the result of an exchange process aiming to maximize benefits and minimize costs. PEI promotes equitable exchanges, enhancing trust and cooperation. In contrast, NEI may involve exploitative exchanges, eroding trust and fostering conflict.
- **Interpersonal Emotion Regulation:** Zaki and Williams (2013) discuss how individuals regulate not only their own emotions but also those of others during social interactions. PEI involves empathetic engagement to support others' emotional well-being. NEI may entail manipulating others' emotions for personal gain.

Differentiating PEI and NEI

The distinction between PEI and NEI lies in the individual's motivation and ethical application of emotional competencies:

- **Motivation:** PEI is driven by intrinsic motivation, focusing on personal growth and the well-being of others. NEI is propelled by extrinsic motivation, seeking external rewards or advantages, often at the expense of others.
- **Ethical Application:** PEI entails the ethical use of emotional skills to build and maintain positive relationships. NEI involves the unethical manipulation of emotions to achieve self-serving objectives.
- **Social Outcomes:** PEI leads to trust, collaboration, and emotional well-being within social groups. NEI results in mistrust, conflict, and emotional distress.

Real-World Examples:

- **PEI Example:** A leader who actively listens to team members, empathizes with their concerns, and fosters an inclusive environment demonstrates PEI, leading to increased team cohesion and productivity.
- **NEI Example:** An individual who feigns empathy to extract confidential information for personal advantage exhibits NEI, potentially causing harm to relationships and organizational integrity.

The Dual-Path Model of Emotional Intelligence provides a comprehensive framework for understanding how emotional competencies can lead to divergent social outcomes based on underlying motivations and ethical

considerations. By integrating theories of emotional regulation, motivation, and social interaction, the model underscores the importance of fostering PEI to enhance interpersonal relationships and societal well-being.

APPLICATIONS OF THE DUAL-PATH MODEL OF EMOTIONAL INTELLIGENCE

The Dual-Path Model of Emotional Intelligence (EI), encompassing Positive Emotional Intelligence (PEI) and Negative Emotional Intelligence (NEI), offers a comprehensive framework for understanding how emotional competencies influence behavior across various sectors. This section explores the application of this model in leadership and organizational behavior, healthcare communication, educational environments, and conflict resolution and negotiation.

Leadership and Organizational Behavior

In organizational settings, leaders with high PEI are adept at self-awareness, self-regulation, empathy, social skills, and intrinsic motivation. These competencies enable them to inspire trust, communicate effectively, and foster a positive work environment. Such leaders are more adaptable to change, better at managing stress, and capable of making decisions that balance the needs of multiple stakeholders.

Conversely, leaders exhibiting NEI may use their emotional skills manipulatively, leading to toxic work environments. They might exploit others' emotions for personal gain, resulting in decreased morale and increased turnover. Understanding the dual paths of EI is crucial for organizations aiming to cultivate ethical and effective leadership.

Healthcare Communication

In healthcare, PEI is vital for patient-centered care. Healthcare professionals with high PEI can recognize and regulate their emotions, empathize with patients, and communicate effectively, leading to improved patient satisfaction and outcomes. Active listening, a component of PEI, enables practitioners to understand patients' concerns, including unspoken fears or expectations, enhancing trust and adherence to treatment plans.

However, NEI in healthcare can be detrimental. Practitioners who manipulate patient emotions or fail to manage their own stress can compromise patient care. Thus, fostering PEI through training and organizational support is essential for effective healthcare communication.

Educational Environments

Educators with high PEI create supportive learning environments by understanding and managing their emotions, demonstrating empathy, and fostering positive relationships with students. Programs like RULER (Recognizing, Understanding, Labeling, Expressing, and Regulating emotions) have been implemented to enhance emotional intelligence in schools, leading to improved academic performance and social-emotional competence.

In contrast, educators displaying NEI may misuse their emotional skills, leading to classroom conflicts and a negative learning atmosphere. Training teachers in emotional regulation and empathy is crucial to prevent such outcomes and promote a positive educational environment.

Conflict Resolution and Negotiation

Emotional intelligence plays a significant role in conflict resolution and negotiation. Individuals with high PEI can de-escalate tense situations, facilitate productive dialogue, and find mutually beneficial solutions. They manage their emotions effectively, preventing personal biases from exacerbating conflicts.

NEI, however, can lead to manipulative tactics in negotiations, undermining trust and collaboration. Training in emotional intelligence, focusing on self-awareness, empathy, and ethical behavior, is essential for effective conflict management across various sectors.

The Dual-Path Model of Emotional Intelligence underscores the importance of ethical application of emotional competencies across different sectors. By fostering PEI and mitigating NEI, organizations can enhance leadership effectiveness, healthcare communication, educational outcomes, and conflict resolution strategies. Implementing training programs and organizational policies that promote PEI is vital for achieving these goals.

IMPLICATIONS FOR RESEARCH AND PRACTICE

The Dual-Path Model of Emotional Intelligence (EI), distinguishing between Positive Emotional Intelligence (PEI) and Negative Emotional Intelligence (NEI), provides a nuanced framework for understanding emotional competencies in various professional contexts. This section explores practical strategies for enhancing PEI and mitigating NEI, and discusses the implications for human resources (HR), training programs, and policy-making.

Practical Strategies for Developing PEI and Mitigating NEI

Enhancing PEI involves cultivating self-awareness, self-regulation, empathy, motivation, and social skills. Practical strategies include:

- **Self-Awareness**: Encouraging individuals to maintain emotional journals can help identify emotional triggers and patterns, fostering greater self-understanding (Aken, 2024).
- **Self-Regulation**: Engaging in mindfulness practices has been shown to enhance self-regulation and effectively reduce stress levels. Mindfulness-Based Stress Reduction (MBSR) programs, in particular, have demonstrated efficacy in improving emotional regulation and decreasing psychological distress. For instance, a study by Goldin et al. (2014) found that MBSR training in patients with social anxiety disorder led to reduced emotional reactivity and enhanced emotion regulation.
- **Empathy and Social Skills**: Engaging in active listening exercises and role-playing scenarios can enhance interpersonal understanding and communication (McNaughton et al., 2008).

To mitigate NEI, organizations can:

- **Promote Ethical Awareness**: Incorporate discussions on the ethical use of emotional skills in training programs to prevent manipulative behaviors (Côté et al., 2011).
- **Establish Feedback Mechanisms**: Implement 360-degree feedback systems to identify and address negative emotional behaviors in the workplace (HBS Online, 2021).

Implications for Human Resources and Training Programs

Human Resources (HR) departments are instrumental in embedding emotional intelligence (EI) within organizational culture. By integrating EI competencies into recruitment processes, performance evaluations, and leadership development programs, HR can cultivate a workforce that is not only skilled but also emotionally adept, leading to enhanced organizational effectiveness (Goleman, 1998; Mayer & Salovey, 1997).

Training programs should be designed to:

- **Enhancing Emotional Intelligence (EI) in the Workplace**
  Organizations can cultivate a more emotionally adept workforce by implementing targeted strategies to develop both Positive Emotional Intelligence (PEI) and Negative Emotional Intelligence (NEI) competencies.

- **Developing Positive Emotional Intelligence (PEI) Skills**
  To foster PEI, organizations should offer workshops and courses that focus on developing key emotional competencies such as empathy and self-regulation. These programs aim to enhance emotional intelligence, empathy, and emotion regulation, leading to improved interpersonal relationships and overall organizational effectiveness (Mayer et al., 2004).
- **Addressing Negative Emotional Intelligence (NEI) Behaviors**
  Equally important is providing training on recognizing and mitigating manipulative emotional tactics. This approach promotes ethical interpersonal interactions and helps in managing workplace dynamics effectively (Goleman, 1998).
- **Integrating EI Assessments in Recruitment**
  Moreover, incorporating EI assessments during hiring processes can help identify candidates with strong emotional competencies. Utilizing tools like the Mayer–Salovey–Caruso Emotional Intelligence Test (MSCEIT) allows organizations to evaluate candidates' abilities to perceive, use, understand, and regulate emotions, contributing to a more harmonious work environment (Mayer et al., 2002).

Policy-Making and Organizational Culture

At the policy level, organizations should:

- **Develop EI-Centric Policies**: Creating policies that prioritise emotional intelligence (EI) is critical for promoting effective leadership and cohesive team dynamics. By incorporating EI competencies into organisational standards, HR departments can create environments that foster empathy, self-regulation, and interpersonal skills, resulting in enhanced cooperation and overall organisational performance (Miswanto, Soares, Da Silva, Biyanto, & Winarno, 2024).

- **Promote Psychological Safety**: Establishing psychological safety within the workplace is crucial for fostering an environment where employees feel secure to express their emotions and provide feedback without fear of negative repercussions. This sense of safety not only enhances individual well-being but also promotes organizational effectiveness by encouraging open communication and continuous learning (Edmondson, 1999; Kahn, 1990).

By institutionalizing EI principles, organizations can enhance employee engagement, reduce turnover, and improve overall performance.

FUTURE RESEARCH DIRECTIONS

The Dual-Path Model of Emotional Intelligence (EI), distinguishing between Positive Emotional Intelligence (PEI) and Negative Emotional Intelligence (NEI), offers a nuanced framework for understanding the multifaceted nature of EI. To advance this theoretical model, future research should focus on empirical testing, interdisciplinary studies, and refining and validating the model.

Suggestions for Empirical Testing of the model

***Development of Measurement Instruments*:** Creating reliable and valid instruments to measure PEI and NEI is crucial. While existing EI assessments like the Mayer-Salovey-Caruso Emotional Intelligence Test (MSCEIT) focus on overall EI, they do not differentiate between its positive and negative applications. Developing scales that specifically assess PEI and NEI will enable researchers to empirically test the dual-path model.

Longitudinal Studies: Conducting longitudinal research can provide insights into how PEI and NEI develop and change over time. Such studies can examine the stability of these constructs and their impact on various life outcomes, including career progression, relationship satisfaction, and mental health.

***Experimental Designs*:** Implementing experimental studies can help establish causal relationships between PEI/NEI and specific behaviors or outcomes. For example, interventions designed to enhance PEI can be tested for their effectiveness in improving teamwork and reducing workplace conflicts.

Potential Interdisciplinary Studies

***Neuroscience*:** Exploring the neural correlates of PEI and NEI can deepen our understanding of the biological underpinnings of emotional intelligence. Functional magnetic resonance imaging (fMRI) studies can identify brain regions associated with the positive and negative applications of EI.

***Organizational Behavior*:** Investigating how PEI and NEI influence organizational dynamics, leadership styles, and employee well-being can provide practical insights for businesses. Such studies can inform the development of training programs aimed at fostering ethical leadership and reducing manipulative behaviors.

***Education*:** Examining the role of PEI and NEI in educational settings can shed light on their impact on teaching effectiveness, student engagement, and classroom climate. Research in this area can guide the integration of EI training into teacher education programs.

***Healthcare*:** Studying the effects of PEI and NEI on patient-provider interactions can inform strategies to improve patient satisfaction and outcomes. For instance, enhancing PEI among healthcare professionals may lead to better communication and empathy towards patients.

Recommendations for Refining and Validating the Model

***Theoretical Clarification*:** Further conceptual work is needed to delineate the boundaries between PEI and NEI. Clarifying these constructs will aid in developing precise measurement tools and interventions.

***Cross-Cultural Validation*:** Testing the dual-path model across different cultural contexts can determine its universality and identify cultural factors that influence the expression of PEI and NEI. Such research can ensure the model's applicability in diverse settings.

***Integration with Existing Theories*:** Aligning the dual-path model with established psychological theories, such as social learning theory and cognitive-behavioral theory, can provide a comprehensive framework for understanding the development and application of EI.

***Practical Applications*:** Developing and evaluating interventions aimed at enhancing PEI and mitigating NEI can validate the model's utility. For example, training programs that focus on empathy development and ethical decision-making can be assessed for their effectiveness in promoting PEI.

Advancing the Dual-Path Model of Emotional Intelligence requires a multifaceted research approach. Empirical testing through the development of specific measurement tools, longitudinal and experimental studies, interdisciplinary collaborations, and theoretical refinements will enhance our understanding of PEI and NEI. Such efforts will not only validate the model but also inform practical applications across various sectors, including education, healthcare, and organizational development.

CONCLUSION

The Dual-Path Model of Emotional Intelligence (EI), distinguishing between Positive Emotional Intelligence (PEI) and Negative Emotional Intelligence (NEI), offers a nuanced framework for understanding the multifaceted nature of EI. This model underscores the dual capacity of EI to foster both constructive and potentially detrimental outcomes, depending on its application.

The Dual-Path Model emphasizes that EI is not inherently beneficial or harmful; rather, its impact is contingent upon how individuals utilize their emotional competencies. PEI involves the ethical and empathetic use of

emotional skills to enhance interpersonal relationships, promote well-being, and facilitate positive organizational outcomes. Conversely, NEI refers to the manipulation of emotional understanding for self-serving purposes, which can lead to unethical behavior and interpersonal discord.

Understanding this dichotomy is crucial in various sectors, including healthcare, education, and organizational leadership. For instance, in healthcare settings, high levels of trait emotional intelligence (TEI) have been linked to reduced burnout and increased work engagement among professionals. Similarly, in organizational contexts, EI contributes to ethical decision-making and fosters a positive work environment.

Emphasis on Ethical Application of EI

The ethical application of EI is paramount to harnessing its benefits while mitigating potential harms. Developing PEI involves cultivating self-awareness, empathy, and emotional regulation to navigate complex social interactions responsibly. Organizations can promote PEI by integrating EI training into professional development programs, emphasizing ethical considerations, and establishing feedback mechanisms to identify and address manipulative behaviors.

Research indicates that individuals with higher EI levels exhibit greater ethical behavior, integrating emotional awareness into decision-making processes. This ethical dimension of EI is essential in leadership roles, where decisions can significantly impact organizational culture and stakeholder well-being.

Broader Social Implications

The implications of the Dual-Path Model extend beyond individual and organizational levels, influencing broader societal dynamics. In educational environments, incorporating social-emotional learning (SEL) programs can foster empathy and compassion among students, leading to improved academic performance and reduced behavioral issues. In the realm of artificial intelligence, the development of emotional AI technologies raises ethical concerns regarding the manipulation of emotions and the potential erosion of genuine human interactions. Moreover, the ethical application of EI contributes to social cohesion by promoting understanding and cooperation across diverse groups. Conversely, the misuse of EI for manipulative purposes can exacerbate social tensions and undermine trust within communities.

The Dual-Path Model of Emotional Intelligence provides a comprehensive framework for understanding the complex role of EI in human behavior. By distinguishing between its positive and negative applications, the model highlights the importance of ethical considerations in the development and utilization of emotional competencies. Emphasizing the cultivation of PEI while mitigating NEI can lead to enhanced individual well-being, ethical

organizational practices, and a more empathetic society. Future research and practical applications should continue to explore strategies for fostering PEI and addressing the challenges associated with NEI to fully realize the potential of emotional intelligence in various domains.

REFERENCES

1. Austin, E. J., Farrelly, D., Black, C., & Moore, H. (2007). *Emotional intelligence, Machiavellianism and emotional manipulation: Does EI have a dark side?* Personality and Individual Differences, 43(1), 179–189.
2. Bar-On, R. (1997). *Bar-On Emotional Quotient Inventory (EQ-i): Technical manual*. Multi-Health Systems.
3. Cherry, K. (2018). *Emotional intelligence theories & components explained*. Positive Psychology. Retrieved from https://positivepsychology.com/emotional-intelligence-theories/
4. Cherniss, C. (2010). *Emotional intelligence: Toward clarification of a concept*. Industrial and Organizational Psychology, 3(2), 110–126.
5. Côté, S., DeCelles, K. A., McCarthy, J. M., Van Kleef, G. A., & Hideg, I. (2011). *The Jekyll and Hyde of emotional intelligence: Emotion-regulation knowledge facilitates both prosocial and interpersonally deviant behavior*. Psychological Science, 22(8), 1073–1080.
6. Deci, E. L., & Ryan, R. M. (1985). *Intrinsic motivation and self-determination in human behavior*. Springer Science & Business Media.
7. Goleman, D. (1995). *Emotional Intelligence: Why It Can Matter More Than IQ*. Bantam Books.
8. Goleman, D. (1998). *Working with emotional intelligence*. Bantam Books.
9. Goldin, P. R., Ziv, M., Jazaieri, H., Hahn, K., & Gross, J. J. (2014). MBSR training in patients with social anxiety disorder: Effects on emotion regulation and attention. *Journal of Cognitive Psychotherapy*, *28*(1), 3–12.
10. Gross, J. J. (1998). *The emerging field of emotion regulation: An integrative review*. Review of General Psychology, 2(3), 271–299.
11. Homans, G. C. (1958). *Social behavior as exchange*. American Journal of Sociology, 63(6), 597–606.
12. Lopes, P. N., Brackett, M. A., Nezlek, J. B., Schütz, A., Sellin, I., & Salovey, P. (2004). *Emotional intelligence and social interaction*. Personality and Social Psychology Bulletin, 30(8), 1018–1034.
13. Lopes, P. N., Salovey, P., Côté, S., & Beers, M. (2004). *Emotion regulation abilities and the quality of social interaction*. Emotion, 5(1), 113–118.
14. Lopes, P. N., Salovey, P., & Straus, R. (2003). *Emotional intelligence, personality, and the perceived quality of social relationships*. Personality and Individual Differences, 35(3), 641–658.

15. Mayer, J. D., & Salovey, P. (1997). *What is emotional intelligence?*. In P. Salovey & D. J. Sluyter (Eds.), *Emotional development and emotional intelligence: Educational implications* (pp. 3–31). Basic Books.
16. Mayer, J. D., Salovey, P., & Caruso, D. R. (2004). Emotional intelligence: Theory, findings, and implications. *Psychological Inquiry*, 15(3), 197–215. https://doi.org/10.1207/s15327965pli1503_02
17. Mayer, J. D., & Salovey, P. (1990). *Emotional intelligence*. Imagination, Cognition and Personality, 9(3), 185–211.
18. Mayer, J. D., Salovey, P., & Caruso, D. R. (2004). *Emotional intelligence: Theory, findings, and implications*. Psychological Inquiry, 15(3), 197–215.
19. Mayer, J. D., Salovey, P., & Caruso, D. R. (2002). *MSCEIT: Mayer–Salovey–Caruso Emotional Intelligence Test*. Multi-Health Systems.
20. Miswanto, M., Soares, A. R. C., Da Silva, F. M., Biyanto, F., & Winarno, W. W. (2024). Integration of team performance, emotional intelligence, and human resource management practices: A systematic review. *International Journal of Asian Business and Management, 3*(4), 425–442. https://doi.org/10.55927/ijabm.v3i4.10760
21. O'Boyle, E. H., Humphrey, R. H., Pollack, J. M., Hawver, T. H., & Story, P. A. (2011). *The relation between emotional intelligence and job performance: A meta-analysis*. Journal of Organizational Behavior, 32(5), 788–818.
22. Ryan, R. M., & Deci, E. L. (2000). *Self-determination theory and the facilitation of intrinsic motivation, social development, and well-being*. American Psychologist, 55(1), 68–78.
23. Salovey, P., & Mayer, J. D. (1990). *Emotional intelligence*. Imagination, Cognition and Personality, 9(3), 185–211.
24. Schutte, N. S., Malouff, J. M., Hall, L. E., Haggerty, D. J., Cooper, J. T., Golden, C. J., & Dornheim, L. (2001). *Development and validation of a measure of emotional intelligence*. Personality and Individual Differences, 25(2), 167–177.
25. University Canada West. (2023, June 9). *The importance of emotional intelligence in the workplace*. Retrieved from https://www.ucanwest.ca/blog/education-careers-tips/the-importance-of-emotional-intelligence-in-the-workplace.
26. Edmondson, A. (1999). Psychological safety and learning behavior in work teams. Administrative Science Quarterly, 44(2), 350–383.
27. Kahn, W. A. (1990). Psychological conditions of personal engagement and disengagement at work. Academy of Management Journal, 33(4), 692–72
28. Zaki, J., & Williams, W. C. (2013). *Interpersonal emotion regulation*. Emotion, 13(5), 803–810

The Role of Schiff Bases in Drug Discovery through Bioinformatics Approaches

Işık ÇAKMAK[1]
Nurhan GÜMRÜKÇÜOĞLU[2]

1- Dr ; Biostatistics and Medical Informatics, Karadeniz Technical University, Trabzon, Türkiye isikozdinc@gmail.com. ORCID No: 0000-0003-4758-4077
2- Prof. Dr.; Department of Medical Services and Techniques, Vocational School of Health Sciences, Karadeniz Technical University, Trabzon, Türkiye ngumrukcuoglu@ktu.edu.tr ORCID No: 0000-0002-9669-6318

ABSTRACT

Schiff bases are compounds formed by the reaction of primary amines with carbonyl compounds and are known to possess structural diversity and broad biological activity. These compounds exhibit antioxidant, antimicrobial, anticancer, antiviral, antimalarial and anti-inflammatory properties. Their biological activity is generally enhanced when they form complexes with metal ions. Recent studies have combined experimental and computational methods to investigate the therapeutic potential of Schiff bases. Molecular docking and molecular dynamics simulations have revealed strong binding interactions between Schiff base derivatives and various biological targets, including viral proteins and cancer-related enzymes. Furthermore, ADMET and QSAR analyses provided insight into their pharmacokinetic behaviour and toxicity profiles. In silico techniques contribute significantly to drug discovery by predicting molecular interactions, reducing the need for extensive laboratory testing and saving time and resources. Supported by both biological experiments and computational data, Schiff bases have emerged as promising candidates for the development of novel therapeutics. Their versatility and efficacy indicate a strong potential for further applications in the treatment of infectious diseases, cancer and neurological disorders.

Keywords – Schiff Bases, Biological Activity, Molecular Docking, Drug Discovery, In Silico Analysis.

INTRODUCTION

Schiff bases were first synthesised in 1864 by U. SCHIFF from the reaction of primary amines with aldehydes and ketones and were named Schiff base in memory of the synthesiser. Schiff bases are compounds formed by the condensation reaction of carbonyl compounds and primary amines and carry a characteristic azomethine group (-CH=N-) in their structure. Figure 1 shows the formation reaction of Schiff bases (Schiff, 1864).

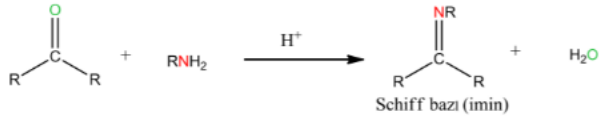


Figure 1. General representation of Schiff Base (Imine) synthesis

These compounds are widely used in biological applications thanks to their stable structures and easy synthesis. Especially in recent years, studies have revealed that Schiff bases exhibit versatile biological activities.

Pyridoxal in the structure of N-alkylsalicylaldehyde, which can give Schiff base, has shed light on basic molecules with important properties. Its structure is shown in Figure 2. An imine linkage formed between the aldehyde derivative of vitamin A and the opsin protein in the retina plays a critical role in visual signal transduction. Vitamins often function as coenzymes, meaning they assist enzymatic activities by binding to specific enzymes—large protein molecules that accelerate chemical transformations in the cell. A notable biologically active aldehyde is pyridoxal phosphate, the coenzymatically active form of vitamin B6. This compound forms a Schiff base (imine bond) with amino acid residues within enzymes, allowing it to participate in key reactions. One such reaction is transamination, which involves transferring an amino group from one amino acid to another, a process essential for amino acid metabolism and synthesis. Ultimately, enzymatic hydrolysis breaks the bond between the pyridoxal group and the modified amino acid. The regenerated pyridoxal then binds with a phosphate group, forming pyridoxal phosphate again (Rafique et al., 2022).

Imine is formed as a result of the reaction of the aldehyde group of pyridoxal phosphate and the amino acid in the enzyme. In addition, as a result of the binding of the phosphate group in the structure to another part of the enzyme, the imine bond is opened due to the action of an amino acid on the enzyme system and itself is bound. Thus, a new imine is formed and this imine hydrolyses to form pyridoxamine (Canpolat, 2003).

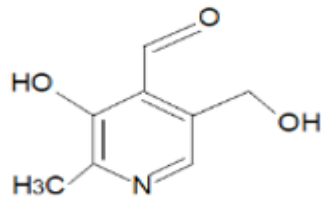


Figure 2. Pyridoxal (vitamin B6)

In the study by Uddin et al., The molecular docking of one of the synthesised Schiff base ligands with the SARS-CoV-2 receptor protein was analysed. The results revealed that this ligand showed higher binding affinity than hydroxychloroquine (HCQ). ADMET analyses showed that the ligand is non-carcinogenic and has lower toxicity than HCQ. These findings suggest that these Schiff bases can be evaluated as potential inhibitors against COVID-19 (Uddin et al., 2021).

The newly synthesised imine derivative N-allyl-2-(2-oxoacenaphthylene-1(2H)-ylidene)hydrazine-1-carbothioamide was characterised by different spectral techniques and complexes were synthesised. The antioxidant activity investigation showed that the ligand

and Zn (II) complex have high activity compared to other complexes with 88.5% and 88.6%, respectively. Accordingly, the antitumour activity of the isolated compounds was studied against hepatocellular carcinoma cell line (HepG2) exhibiting IC50 6.45 ± 0.25 and 6.39 ± 0.18 μM, respectively (Melha et al., 2021).

In the study conducted by Al-Wahaibi et al. (2018); the structures of coumarin (2H-1-benzopyran-2-one; 2H-chromen-2-one) derivatives have been studied in detail. It was determined that these compounds may be potential drug candidates with a broad spectrum of biological effects by interacting with various enzymes and receptors in organisms through weak bond interactions. It was emphasised that naturally occurring compounds such as novobiocin, chlorobiocin and coumarin represent a unique class of antibiotics that are particularly effective against Gram positive bacteria. The anticancer potential of coumarin derivatives has also attracted attention; STX 64 derivative, a potent estrogen antagonist, has been reported in clinical trials as an effective agent against breast cancer. In addition, auraptin compound has been reported to show anticancer effects against liver, skin, tongue, oesophagus and colon cancers (Al-Wahaibi, Abu-Melha & Ibrahim, 2018).

Goud and his friends (2019) stated that cancer is a serious disease progressing with uncontrolled cell growth and new anticancer agents are needed due to problems such as toxicity and low selectivity despite current treatments. In this study, biologically active 1,2,3-triazole derivatives and coumarin-triazole hybrid compounds targeting Galectin-1 (Gal-1) were synthesised and characterised by spectral methods. These compounds showed potent antiproliferative and cytotoxic effects on bone, lung, breast, colon and liver cancer cell lines (Goud et al., 2019).

In recent studies, it has been reported that various Schiff bases such as benzothiazole and isatin are effective against Gram-positive and Gram-negative bacteria, and the activity increases when combined with some metal complexes (Jorge et al., 2024; Ceramella et al., 2024). The complexes formed by tridentate Schiff bases synthesised from O vanillin and phenylurea derivatives with Mn, Co, Ni, Cu, Zn and Zr were evaluated against both bacterial/fungal activity and HCT 116 and MCF 7 cancer cell lines; many complexes showed antibacterial and antitumour effects. In the same metal complex study (O vanillin + phenylurea), tridentate ligands were reported to be cytotoxic in both colon and breast cancer cells (Hassan et al., 2022).

However, some imidazopyridine-Schiff base derivatives have been considered as examples of heterocyclic structures with anticancer potential (Azzouzi et al., 2024). Different Schiff base composites have been studied especially as antibacterial agents. Fe^{2+} and Co^{2+} forms of Schiff base metal complexes composed of vanillin tryptophan showed high activity against

Gram-negative pathogens such as E. coli, Shigella and S. Typhi (Abubakar et al., 2022).

In a article published in 2024, imidazopyridine Schiff base compounds were described to show both antiviral activity against HIV in vitro and binding to RNA virus proteins at the molecular level. This study was supported by both experimental and in silico methods (Azzouzi et al., 2024).

In in vitro tests on Plasmodium falciparum strains with pyrazole Schiff base hybrids, EC_{50} values were reported between 1.95-1.98 µg/ml and found effective (Aggarwal et al., 2018).

In a study conducted in 2019, it was reported that benzimidazole Schiff bases showed antiplasmodial activity, some compounds stood out by providing 85-95% growth inhibition; IC_{50} values were measured approximately 27-28 µg/ml (Fonkui et al., 2019).

Imidazole-based Schiff bases have attracted the attention of researchers due to their strong therapeutic properties and have contributed to the development of many chemotherapeutic agents such as anticancer, antimicrobial, antioxidant, antiviral, antileishmanial in recent years (Figure 3) (Gopalakrishnan, Angamaly & Velayudhan, 2021).

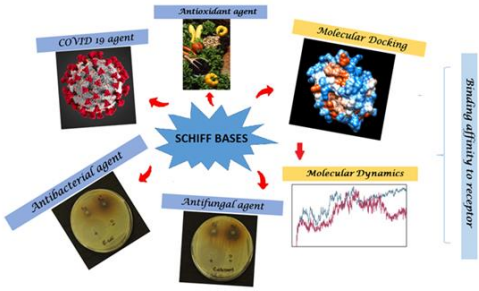


Figure 3: Evaluation of diverse biological activities of Schiff bases by in silico analysis.

In a recent study, the antimicrobial activity of Schiff base complex was tested on some bacteria and Candida albicans. Growth inhibition of 11-15.5 mm in diameter was observed at high concentrations (2-2.5 mg/mL), especially on C. albicans (Rajimon et al., 2025).

In another study, the Schiff base ligand HIPB and its palladium(II) (C1), platinum(II) (C2) and zinc(II) (C3) complexes were synthesised and characterised. Theoretical studies have shown that the C2 complex is the most reactive and pharmacologically most potent. In biological tests, all complexes suppressed HCT116 colon cancer cells, while C2 showed the highest anticancer and antioxidant effect. In the interaction studies with catalase enzyme, the complexes showed mixed type of inhibition, with the strongest inhibition by C1 (82.2%). Fluorescence quenching and molecular

docking analyses showed that binding occurs by dynamic mechanism and hydrophobic interactions. Especially C1 caused the most changes in the structure of the enzyme (Keikha et al., 2025).

Chitosan conjugates (CSBs) with biologically active Schiff bases were synthesised. These structures have been extensively studied in the literature due to their both catalytic and biological (anticancer, anti-inflammatory, antioxidant and especially antimicrobial) activities (Iacopetta et al., 2025).

In a recent study, it was reported that imine and hydroxyl groups of salicylaldehyde-based Schiff bases play a key role in the mechanism of biological activities and phenyl-derived metal complexes show higher antimicrobial activity due to their lipophilicity and delocalised π-electrons. In addition, chelate formation increases lipophilicity by reducing the polarity of the metal ion, which facilitates passage through the cell membrane and increases the antimicrobial and anticancer effect by enzyme inhibition (Rana et al., 2025).

In another study in 2025, Fe (III) and Ce (III) complexes synthesised from 2-hydroxy-1-naphthaldehyde and L-histidine-derived Schiff base ligand were characterised and their biological activities were investigated. The compounds showed antiviral (HSV-1, CV-B4, Adeno-7), anticancer, antioxidant and antifungal effects (Taha et al., 2025).

Artificial intelligence (AI), which enables the development of computer systems capable of learning from data inputs, is an important branch of computer science and first appeared in the field of bioinformatics and enabled the use of machine learning algorithms in the analysis of large-scale genomic and proteomic data (Ercan & Tıraş, 2025). Artificial intelligence is widely applied in drug discovery (Tarı & Arpacı, 2024).

Bioinformatics is an interdisciplinary science that enables the collection, processing, sharing and creation of new biological data and uses computer software in this process (Kartal et al., 2023).

Despite advances in disease biology and technological developments, bringing new drugs to the market is still a costly, time-consuming and challenging process. This process involves many complex factors such as failures in clinical trials, the need for drugs to overcome physiological barriers to reach targets, the effect of genetic differences on drug responses and off-target toxicities. New ideas and innovative approaches are required to overcome these challenges and accelerate drug discovery processes. In this context, computer-aided drug design has long been seen as a promising option, while recently, artificial intelligence-based methods offer potential solutions to this process (Çelik et al., 2021).

Drug discovery is a process carried out with the aim of improving human health. The traditional drug discovery process is usually time-consuming, costly and involves experimental studies. Therefore, scientists and researchers are in search of new methods to speed up the drug discovery

process and make it more efficient. Computational drug discovery has attracted great interest in the field of drug discovery in recent years.

Computational methods have been a valuable tool in areas such as the design of drug candidate compounds, determination of their molecular properties, understanding of interaction mechanisms and drug candidate selection. Computational approaches such as molecular modelling, simulation techniques, virtual screening and machine learning can be used rapidly, economically and efficiently in drug discovery (Hashemian & Özcan, 2024).

Structural bioinformatics is a crucial tool for predicting the binding patterns and strengths of drug molecules with identified targets. Molecular docking simulations, binding energy calculations and molecular dynamics simulations provide valuable information about the interactions between drugs and target sites. This helps to select drug candidates and increase their binding specificity and efficacy (Dokumacı, 2024).

Computer-aided drug design uses the computational principle by applying it to chemistry to discover, develop or study drugs and biologically active molecules associated with drugs. Molecular docking, one of the computational methods, is a process that tries to predict the non-covalent/covalent binding of a macromolecule (receptor) and a small molecule (ligand) (Enisoğlu & Ayık, 2022).

In a study, the synthesised compound 2-((4-(dimethylamino)benzylidene)amino)-5-methylphenol was analysed by bioinformatic methods for its possible inhibitory effects on JNK1 enzyme. Molecular docking simulations revealed that the compound showed high binding affinity to the active site of the target enzyme and was conformationally favourably located. These interactions are supported by hydrogen bonds and π-π stacking between aromatic systems. The obtained binding energy and docking scores indicate that the compound has a strong potential for JNK1 inhibition (Karaosmanoğlu, Berber & Uysal, 2023). New trifluoromethyl group-containing azo-imine compounds were subjected to computer-assisted molecular docking analysis with different biological target proteins to evaluate their antioxidant potential. In the study, it was determined that these compounds showed strong and stable binding especially with oxidative stress-related proteins. The compounds were found to bind to active sites via hydrogen bonds, van der Waals forces and π-π interactions. The results obtained indicate that these new compounds may be potential therapeutic agents in oxidative stress-related diseases (Yeşil, 2024).

In another study, the interactions of two Schiff base derivatives (E)-2,4-di-tert-butyl-6-((4-fluorophenylimino)methyl)phenol (I) and (E)-2,4-di-tert-butyl-6-((3-iodo-4-methylphenylimino)methyl)phenol (II) with Cannabinoid Receptor 1 (CNR1) were investigated by molecular docking method. In the analyses, the types of ligand-protein bonds and the effects of these bonds on the 3D structure were evaluated, and the physicochemical

properties, pharmacokinetic profiles and drug similarity of the compounds were calculated. As a result, it was determined that iodine-containing compound (II) showed stronger interaction with CNR1 and both compounds could be potential drug candidates by forming stable structures (Güzel, Macit & Yavuz 2023).

A research aims to develop new therapeutic approaches for neurodegenerative diseases, especially Alzheimer's disease. In the study, new Schiff bases derived from (EZ)-N′-benzylidene-(2RS)-2-(6-chloro-9H-carbazol-2-yl)propanhydrazide were obtained by microwave assisted synthesis method. The structures of the synthesised compounds were confirmed using FT-IR and NMR spectroscopy. Bioinformatics, chemicalinformatics and computational pharmacology techniques were used to evaluate the drug-like properties, pharmacokinetic and pharmacodynamic behaviours and pharmacogenomic profiles of these compounds and to predict their possible binding with therapeutic targets. As a result of the analyses, it was determined that all compounds have suitable properties for drug development and may be candidates for neuropsychiatric diseases. In particular, it was revealed that compound 1e has a strong potential in the treatment of neurodegenerative diseases (Avram et al., 2021).

In another study with thiazolidinone-Bis Schiff base compound, the compound was investigated by quantum chemical methods; its structural properties, NLO (nonlinear optical) potential and electron distribution were analysed. Molecular docking studies showed that the compound binds strongly to 4UXL and 4UBF proteins. The high binding energy, especially with 4UBF, indicates that this structure may be a potential drug candidate in cancer and urease targeted therapies (Gören et al., 2024). In another study, Schiff bases with pyrazole skeleton were synthesised and their multiple biological activities were evaluated. One of the compounds stood out especially for its antioxidant, antidiabetic and anti-Alzheimer effects. Another compound showed significant antiarthritic activity. The physico-chemical properties, drug similarities, lipophilic and polar surface properties of these compounds were determined by bioinformatic analyses. The findings indicate that these novel Schiff base-pyrazole derivatives have therapeutic potential as antioxidant, antidiabetic, anti-Alzheimer and antiarthritic agents (Alkahtani et al., 2023).

In another study, a newly synthesised Schiff base molecule named (E)-N-(2-chloropyridin-3-yl)-1-(5-nitro-2-(piperidin-1-yl)-phenyl)-methan-imine was introduced. The structural, chemical, surface and electronic properties of the molecule and its potential biological targets, drug similarity, ADME and toxicity profiles were investigated by bioinformatics and chemicalinformatics methods. In addition, molecular docking studies were performed with SARS-CoV-2 main protease (Mpro). The results showed that the compound was kinetically unstable and chemically reactive, fulfilled the drug similarity criteria and could cross the blood-brain barrier.

Docking scores revealed that the compound may be an Mpro inhibitor and worthy of investigation in laboratory studies (Şahin & Can, 2023). In molecular docking analyses with molecules in which 1, 2, 3-triazole-containing Schiff bases were synthesised and characterised, it was determined that hydrogen bonds and hydrophobic interactions play an important role between ligands and 7BQY protein binding site. Furthermore, superposition analysis and structural activity association (QSAR) studies with the inhibitor N3 showed that the compounds can be evaluated as potential inhibitors.

In silico cytotoxicity analyses with Drug2Way and PASS online software also show that these Schiff bases may be effective against various cancer cell lines. Overall, it has been suggested that these Schiff bases may be potential therapeutic candidates for the treatment of COVID-19 (Said et al.) In this study, novel Schiff base transition metal complexes containing cobalt, copper, nickel and zinc were synthesised and structurally characterised by spectroscopic methods. These structures were evaluated by in silico methods and their potential interactions with biological targets were analysed. In particular, pharmacokinetic and biological activity predictions were made by ADMET and PASS analyses, followed by molecular docking studies and binding energies against targets such as COVID-19 and prostate cancer proteins were calculated. In this context, especially the high negative binding energy of the zinc complex against the COVID-19 protein revealed that such Schiff-based complexes are effective candidates that can be screened directly by in silico approaches in drug discovery processes (Sindhu & Singh, 2024).

In another study, the newly synthesised Schiff base (E)-1-(5-nitro-2-(piperidin-1-yl)phenyl)-N-(4-phenoxyphenyl)methanimine) was evaluated by molecular docking studies against SARS-CoV-2 main protease (Mpro) and showed strong binding affinity (-9.28 kcal/mol). This result indicates that the compound may be a potential antiviral agent on Mpro (Sahin & Dege, 2023).

RESULTS AND DISCUSSION

These studies show that bioinformatics and molecular docking analyses are an effective and reliable approach to predict the interactions of novel Schiff bases and their metal complexes with biological targets.

These analyses performed by in silico methods determine the potential inhibitory properties of these compounds, allowing them to be evaluated as valuable candidates in drug discovery and development processes. In this context, computational studies at the molecular level save time and resources

by guiding laboratory experiments and also play an important role in targeted drug design.

REFERENCES

Abubakar, S., Shallangwa, G. A., & Ibrahim, A. (2022). Syntheses and evaluation of Fe^{2+}, Co^{2+} and Ni^{2+} complexes with derivatives of Vanillin-Tryptophan Schiff base ligand. *arXiv preprint*, arXiv:2301.05021.

Aggarwal, S., Paliwal, D., Kaushik, D., Gupta, G. K., & Kumar, A. (2018). Pyrazole Schiff base hybrids as anti-malarial agents: Synthesis, in vitro screening and computational study. *Combinatorial Chemistry & High Throughput Screening, 21*(3), 194–203. https://doi.org/10.2174/1386207321666180213092911

Alkahtani, H. M., Almehizia, A. A., Al-Omar, M. A., Obaidullah, A. J., Zen, A. A., Hassan, A. S., & Aboulthana, W. M. (2023). In vitro evaluation and bioinformatics analysis of Schiff bases bearing pyrazole scaffold as bioactive agents: Antioxidant, anti-diabetic, anti-Alzheimer, and anti-arthritic. *Molecules, 28*(20), 7125. https://doi.org/10.3390/molecules28207125

Al-Wahaibi, L. H., Abu-Melha, H. M., & Ibrahim, D. A. (2018). Synthesis of novel 1,2,4-triazolyl coumarin derivatives as potential anticancer agents. *Journal of Chemistry*, 2018, 5201374. https://doi.org/10.1155/2018/5201374

Avram, S., Udrea, A. M., Nuta, D. C., Limban, C., Balea, A. C., Caproiu, M. T., Dumitrascu, F., Buiu, C., & Bordei, A. T. (2021). Synthesis and bioinformatic characterization of new Schiff bases with possible applicability in brain disorders. *Molecules, 26*(14), 4160. https://doi.org/10.3390/molecules26144160

Azzouzi, M., Ait Ouchaoui, A., Azougagh, O., El Hadad, S. E., Abou-Salama, M., Oussaid, A., & Rohand, T. (2024). Synthesis, crystal structure, and antiviral evaluation of new imidazopyridine-Schiff base derivatives: In vitro and in silico anti-HIV studies. *RSC Advances, 14*(50), 36902–36918. https://doi.org/10.1039/D4RA04510D

Canpolat, E. (2003). *İmin ve oksim içeren ligandların sentezi, karakterizasyonu ve bu ligandların bazı metal komplekslerinin incelenmesi* (Yayımlanmamış doktora tezi). Fırat Üniversitesi.

Ceramella, J., Iacopetta, D., Catalano, A., Cirillo, F., Lappano, R., & Sinicropi, M. S. (2022). A review on the antimicrobial activity of Schiff bases: Data collection and recent studies. *Antibiotics, 11*(2), 191. https://doi.org/10.3390/antibiotics11020191

Çelik, İ. N., Arslan, F. K., Tunç, R., & Yıldız, İ. (2021). İlaç keşfi ve geliştirilmesinde yapay zekâ. *Ankara Üniversitesi Eczacılık Fakültesi Dergisi, 45*(2), 400–427.

Dokumacı, A. D. (2024). Antibiyotik direncinin aşılması için yeni stratejiler ve ilaç geliştirme çalışmaları: Geleneksel derleme. *Journal of Literature Pharmacy Sciences, 13*(1), 57-68.

Enisoğlu Atalay, V., & Ayık, Y. (2022). Yeni CDK2 inhibitörlerinin keşfedilmesi için bazı piridazin türevi bileşiklerin SAR analizi ve kenetlenme çalışması. *Süleyman Demirel Üniversitesi Fen Bilimleri Enstitüsü Dergisi, 26*(2), 268–274. https://doi.org/10.19113/sdufenbed.1054847

Ercan, N., & Tıraş, S. (2025). Yapay zekânın veteriner klinik biyokimyada yükselişi. *Veteriner Klinik Biyokimya Dergisi,* 140-149.

Fonkui, T. Y., Ikhile, M. I., Njobeh, P. B., & Ndinteh, D. T. (2019). Benzimidazole Schiff base derivatives: Synthesis, characterization and antimicrobial activity. *BMC Chemistry, 13*(1), 127. https://doi.org/10.1186/s13065-019-0642-3

Gopalakrishnan, A. K., Angamaly, S. A., & Velayudhan, M. P. (2021). An insight into the biological properties of imidazole-based Schiff bases: A review. *ChemistrySelect, 6*(40), 10918–10947.

Goud, N. S., Pooladanda, V., Mahammad, G. S., Jakkula, P., Gatreddi, S., Qureshi, I. A., Alvala, R., Godugu, C., & Alvala, M. (2019). Synthesis and biological evaluation of morpholines linked coumarin–triazole hybrids as anticancer agents. *Chemical Biology & Drug Design, 94*(5), 1919–1929.

Gören, K., Bağlan, M., Yıldıko, Ü., & Tahiroğlu, V. (2024). Anti-kanser ve anti-üreaz aktivitesi için tiazolidinon-bis Schiff bazının moleküler yerleştirme ve DFT analizi. *Iğdır Üniversitesi Fen Bilimleri Enstitüsü Dergisi, 14*(2), 822-834.

Güzel, E., Macit, M., & Yavuz, M. (2023). (E)-2,4-di-tert-bütil-6-((4-florofenilimino)metil)fenol ve (E)-2,4-di-tert-bütil-6-((3-iyodo-4-metilfenilimino)metil)fenol bileşikleri için moleküler docking ve ADME çalışmaları. *Karadeniz Fen Bilimleri Dergisi, 13*(3), 997–1011. https://doi.org/10.31466/kfbd.1283044

Hashemian, A., & Özcan, G. (2024). Hesaplamalı ilaç keşfi ve makine öğrenme algoritmaları. *Eskişehir Türk Dünyası Uygulama ve Araştırma Merkezi Bilişim Dergisi, 5*(1), 29–36.

Hassan, A. M., Said, A. O., Heakal, B. H., Younis, A., Aboulthana, W. M., & Mady, M. F. (2022). Green synthesis, characterization, antimicrobial and anticancer screening of new metal complexes incorporating Schiff base. *ACS Omega, 7*(36), 32418–32431.

Iacopetta, D., Catalano, A., Ceramella, J., Mariconda, A., D'Amato, A., Checconi, P., ... & Sinicropi, M. S. (2025). Chitosan-based Schiff bases (CSBs) and their metal complexes: Promising antimicrobial agents. *Molecules, 30*(2), 207.

Jorge, J., Del Pino Santos, K., Timóteo, F., Piva Vasconcelos, R. R., Ignacio Ayala Cáceres, O., Juliane Arantes Granja, I., ... & Rafique, J. (2024). Recent advances on the antimicrobial activities of Schiff bases and their metal complexes: An updated overview. *Current Medicinal Chemistry, 31*(17), 2330–2344. https://doi.org/10.2174/0929867330666230224092830

Karaosmanoğlu, O., Berber, H., & Uysal, Ü. D. (2023). Synthesis, theoretical studies, cytotoxicity of 2-((4-(dimethylamino)benzylidene)amino)-5-methylphenol with potential JNK1 inhibitory activity. *Süleyman Demirel Üniversitesi Sağlık Bilimleri Dergisi, 14*(2), 253–272.

Kartal, C., Bakar, B., Türköz, B. K., & Ötleş, S. (2023). Gıda kaynaklı protein ve biyoaktif peptit eldesi, saflaştırılması ve karakterizasyonunda kullanılan güncel yöntemler ve biyoinformatik yaklaşımlar. *Niğde Ömer Halisdemir Üniversitesi Mühendislik Bilimleri Dergisi, 12*(2), 395-407.

Keikha, A. O., Shahraki, S., Dehghanian, E., & Mansouri-Torshizi, H. (2025). Effect of central metal ion on some pharmacological properties of new Schiff base complexes: Anticancer, antioxidant, kinetic/thermodynamic and computational studies. *Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy, 325*, 125034. https://doi.org/10.1016/j.saa.2024.125034

Melha, K. S. A., Al-Hazmi, G. A., Althagafi, I., Alharbi, A., Keshk, A. A., Shaaban, F., & El-Metwaly, N. (2021). Spectral, molecular modeling, and biological activity studies on new Schiff's base of acenaphthaquinone transition metal complexes.

Bioinorganic Chemistry and Applications, 2021, 6674394. https://doi.org/10.1155/2021/6674394
Rafique B, Kalsoom S, Sajini AA, Ismail H, Iqbal M. (2022). Synthesis, Characterization, Biological Evaluation and DNA Interaction Studies of 4-Aminophenol Derivatives: Theoretical and Experimental Approach. *Molecules*, 27(4), 1352. doi: 10.3390/molecules27041352. PMID: 35209141; PMCID: PMC8879259.
Rajimon, K. J., Almeer, R., Thangaiyan, P., & Thomas, R. (2025). Structural, spectroscopic, and biological properties of an asymmetric Cu (II) Schiff-base complex: Synthesis, DNA/BSA interactions, and antimicrobial potential with experimental and computational insights. *Polyhedron, 265*, 117277. https://doi.org/10.1016/j.poly.2024.117277
Rana, M. S., Rayhan, N. M. A., Emad, A. H., Hossain, M. I., Shah, M. M., Kudrat–E-Zahan, M., ... & Asraf, M. A. (2025). Salicylaldehyde-based Schiff bases and their transition metal complexes: An overview on synthesis and biological activities. *Journal of Coordination Chemistry, 78*(9), 937–1006. https://doi.org/10.1080/00958972.2025.2482231
Said, M. A., Khan, D. J. O., Al-blewi, F. F., Al-Kaff, N. S., Ali, A. A., Rezki, N., Aouad, M. R., & Hagar, M. (2021). New 1,2,3-triazole scaffold Schiff bases as potential anti-COVID-19: Design, synthesis, DFT-molecular docking, and cytotoxicity aspects. *Vaccines, 9*(9), 1012. https://doi.org/10.3390/vaccines9091012
Schiff, H. (1864). Mittheilungen aus dem Universitätslaboratorium in Pisa: Eine neue Reihe organischer Basen. *Justus Liebigs Annalen der Chemie, 131*(1), 118–119. https://doi.org/10.1002/jlac.18641310115
Sindhu, I., & Singh, A. (2024). Experimental and theoretical insight of Schiff base transition metal complexes: Synthesis, characterization, antimicrobial and COVID-19 molecular docking studies. *Research on Chemical Intermediates, 50*, 413–436. https://doi.org/10.1007/s11164-023-05179-
Şahin, S., & Can, N. N. (2023). A Schiff base with polymorphic structure (Z′= 2): Investigations with computational techniques and in silico predictions. *Polycyclic Aromatic Compounds, 43*(10), 9269–9294.
Şahin, S., & Dege, N. (2023). A perspective with in silico medicinal and computational methods to a new Schiff base molecule. *Afyon Kocatepe Üniversitesi Fen ve Mühendislik Bilimleri Dergisi, 23*(4), 883–897. https://doi.org/10.35414/akufemubid.1237445
Taha, R. H., Saleh, A. M., Abbass, L. M., El-Fakharany, E. M., Almutlq, N. J., Hussein, M. F., & Moustafa, S. M. (2025). Impact of Fe (III) and Ce (III) ions on pharmacological properties of novel Schiff base ligand: Anticancer, antiviral, antioxidant, anti-fungal investigations from wallpaper, and computational insights. *Journal of Molecular Liquids, 427*, 127382. https://doi.org/10.1016/j.molliq.2024.127382
Tarı, Ö., & Arpacı, N. (2024). İlaç tasarımında yapay zekâ uygulamaları. *Ankara Üniversitesi Eczacılık Fakültesi Dergisi, 48*(1), 327–365.
Uddin, M. N., Amin, M. S., Rahman, M. S., Khandaker, S., Shumi, W., Rahman, M. A., & Rahman, S. M. (2021). Titanium (IV) complexes of some tetradentate symmetrical bis Schiff bases of 1,6-hexanediamine: Synthesis, characterization, and in silico prediction of potential inhibitor against coronavirus (SARS-CoV-2). *Applied Organometallic Chemistry, 35*(7), e6067. https://doi.org/10.1002/aoc.6067

Yeşil, T. A. (2024). Triflorometil içeren yeni azo-imin bileşikleri: Sentezi, karakterizasyonu, in siliko ve in vitro yöntemlerle antioksidan özelliklerinin araştırılması. *Journal of Natural & Applied Sciences, 28*(3), 460-471.

An Ophthalmological Review of Feline Herpesvirus-1 in Veterinary Practice

B. Taylan KOÇ

Assoc. Prof.; Aydın Adnan Menderes University, Faculty of Veterinary Medicine, Aydın, Türkiye.
btkoc@adu.edu.tr ORCID No: 0000-0002-4279-6233

ABSTRACT

Feline Herpesvirus-1 (FHV-1) stands as a pervasive and clinically significant viral agent, causing substantial ocular disease in domestic cats. Belonging to the *Alphaherpesvirinae* subfamily, FHV-1 creates lifelong latent infections that can reactivate, leading to recurrent illness, often triggered by stress or immunosuppression. This review offers a thorough examination of the etiology, epidemiology, pathogenesis, clinical signs, diagnosis, treatment, and prevention strategies for eye diseases related to FHV-1. The ocular symptoms of FHV-1 vary widely, from minor conjunctivitis to critical conditions like corneal ulceration and stromal keratitis. The presence of dendritic ulcers is considered a definitive sign of the disease, while long-term consequences can include eosinophilic keratitis and the formation of corneal sequestra. The virus is highly contagious in settings with multiple cats, with young kittens and immunocompromised animals being the most vulnerable. Diagnosis is based on clinical signs, often confirmed by laboratory tests like the polymerase chain reaction (PCR), which is the most sensitive method for detecting active viral shedding. When testing is not an option, treatment is frequently started empirically based on the observed clinical symptoms. The core of the therapeutic regimen consists of antiviral medications, such as topical cidofovir and systemic famciclovir, supplemented with antibiotics and anti-inflammatory drugs when necessary. Vaccination serves as the foundation of prevention, which, while not stopping infection entirely, successfully lessens the severity of the illness and reduces viral shedding. Alongside vaccination, minimizing stress and maintaining environmental hygiene are crucial, especially in shelters and households with multiple cats. A clear understanding of FHV-1's biological characteristics and its effects on the eye is vital for successful clinical management. To enhance therapeutic and preventive results for feline populations, further research into the mechanisms of latency and new antiviral approaches is necessary.

Keywords – Feline Herpesvirus-1 (FHV-1); Ocular Infection; Conjunctivitis; Felines; Ophthalmology.

INTRODUCTION

Eye infections are a common finding in both wild and domestic cat populations and can be caused by a multitude of infectious agents. Despite the diversity of pathogens, the clinical signs—such as conjunctivitis, uveitis, eyelid swelling, and excessive tearing—often present in a similar fashion. These symptoms can point to a wide variety of diseases and causative agents. In a clinical setting, it is common for veterinarians to use broad-spectrum treatments based on past experience rather than targeting a specific pathogen. A definitive diagnosis, however, depends on laboratory confirmation or the use of rapid test kits, which is particularly important for viral infections.

In Türkiye, as in many other regions globally, several viral diseases impact the feline population. These infections often spread more quickly among both owned and stray cats compared to their spread in more developed nations. This rapid transmission can be linked to multiple issues, including inadequate care and nutrition in shelters, ineffective quarantine procedures, crowded multi-cat households, neglectful pet ownership, a large and unmanaged stray animal population, and the introduction of street cats into homes without health screenings. As a result, managing the spread of viral diseases in cats throughout Türkiye presents considerable difficulties.

Both worldwide and locally, the viral agents most frequently associated with feline ocular infections are feline herpesvirus (FHV), feline calicivirus (FCV), feline immunodeficiency virus (FIV), feline leukemia virus (FeLV), feline infectious peritonitis virus (FIPV), and feline panleukopenia virus (FPV). Among these viruses, feline herpesvirus is identified as the most prevalent cause of eye infections. This chapter provides an in-depth overview of feline herpesvirus, the leading viral pathogen in the field of feline ophthalmology.

Feline Herpesvirus-1

Etiology

The order *Herpesvirales* contains the family *Herpesviridae*, which is separated into three subfamilies: *Alphaherpesvirinae*, *Betaherpesvirinae*, and *Gammaherpesvirinae*. Within the *Alphaherpesvirinae*, there are five genera: *Simplexvirus*, *Varicellovirus*, *Mardivirus*, *Iltovirus*, and *Scutavirus*. Felid alphaherpesvirus 1 (FeHV-1), also widely known as feline herpesvirus-1, belongs to the *Varicellovirus* genus (Gatherer et al., 2021:001673).

All herpesviruses are etiologically similar. They possess a linear, double-stranded DNA (dsDNA) genome contained within an icosahedral capsid, which is surrounded by an amorphous tegument and a glycoprotein-spiked envelope. The size of these enveloped viral particles is between 150–

200 nm, and they feature peplomers approximately 8 nm long (Gatherer et al., 2021:001673). The capsid is composed of 12 pentavalent and 150 hexavalent capsomers and is encased in a tegument matrix (Gaskell et al., 2007:339; Maeda et al., 1997:170). Herpesviruses are known to encode around 74 distinct proteins (Maeda et al., 1997:170; Maes, 2012:495830). Their genome is organized into Unique Long (UL) and Unique Short (US) regions, which are flanked by inverted repeats (Grail et al., 1991:222; Rota et al., 1986:59).

Feline herpesviruses produce eight distinct glycoproteins: gB, gC, gD, gE, gG, gH, gI, and gL. Of these, gC is responsible for attaching to the cell surface, whereas gD is believed to provide the capacity for feline-specific binding (Maes et al., 2012:495830). To achieve membrane fusion and enter the host cell, FHV-1 employs a coordinated complex of glycoproteins gB, gH, and gL. While gB serves as the main fusogen, it must be activated by the gH/gL heterodimer, a process initiated when gD interacts with the host's nectin-1 receptor. This cascade of activation (gD → gH/gL → gB) is a conserved mechanism among alphaherpesviruses and is crucial for viral entry (Heldwein and Krummenacher, 2008:1655; Mettenleiter, 2004:169).

Conversely, gE and gI join to form an Fc-binding heterodimer that helps the virus evade the immune system by binding antibodies in a non-functional way, a tactic known as "antibody bipolar bridging" (Johnson and Maggs, 2005:95). Furthermore, the gE/gI complex facilitates cell-to-cell spread, which allows the virus to move between cells without exposure to the extracellular environment, thereby avoiding neutralizing antibodies. This mechanism is vital for virulence *in vivo* but is not required *in vitro* (Mijnes et al., 1997:8399). The most immunogenic of the viral glycoproteins are gB and gD, as they trigger strong neutralizing antibody responses. For this reason, they are key ingredients in subunit and recombinant FHV-1 vaccines, which are designed to prevent the viral attachment and fusion processes (Gaskell et al., 2007:339).

Epidemiology

Infections with Feline Herpesvirus (FHV) spread with remarkable speed throughout domestic and stray cat populations. Transmission is most common in environments where cats are housed in large groups, such as animal shelters (Andrews, 2001:9; Gould, 2011:334). Studies have indicated that the prevalence of FHV-1 infection within the global cat population is over 90% (Andrews, 2001:9; Gould, 2011:334). The virus is primarily transmitted through the nasal, oral, and conjunctival mucous membranes. Other transmission routes include close contact, sharing common spaces, and exposure to airborne aerosols. The occurrence of FHV-1 is notably higher in neonatal kittens (one month old or younger) and in cats that are immunosuppressed or otherwise weakened (Maes, 2012:495830).
The detailed pathways of transmission are as follows:

- ***Direct Contact:*** FHV-1 is most effectively transmitted through direct contact with infectious secretions from the mouth, nose, or eyes. This typically happens during activities like grooming, nuzzling, fighting, or other close interactions between felines (Gaskell et al., 2007:335; Maggs, 2005:97).

- ***Fomites (Indirect Contact):*** FHV-1 is relatively delicate outside a host, but it can remain viable for as long as 18 hours on contaminated surfaces if they are moist (Stiles, 2003:18). Items such as shared food bowls, litter boxes, bedding, grooming equipment, and even the hands and clothing of humans can act as fomites, particularly in shelters or homes with multiple cats (Gaskell et al., 2007:340).

- ***Aerosolization:*** When an infected cat sneezes, it releases aerosolized droplets that contain viral particles. Although this method is less effective for long-distance transmission, it is a very efficient way for the virus to spread in enclosed areas like catteries or shelters (Gaskell et al., 2007:340).

- ***Latent Carriers & Viral Reservoir:*** Nearly all cats that survive an FHV-1 infection will carry the virus for life in a latent state, usually within the trigeminal ganglion. These carrier cats can shed the virus from time to time, particularly when stressed, which helps the virus persist within the general cat population (Maggs, 2005:97).

- ***Control Implications:*** Given the widespread presence of latent carriers and their capacity for unpredictable viral shedding, vaccination is crucial for lessening the severity of clinical symptoms (Gaskell et al., 2007:353). Stress reduction and meticulous hygiene are equally important control measures.

Pathogenesis / Ophthalmic Clinic Observation

Once the virus enters the host, it begins its initial replication in the nasopharynx, tonsils, conjunctiva, trachea, and mandibular lymph nodes (Gaskell et al., 2007:345). Infected cats typically start showing clinical signs after an incubation period of 24 to 48 hours. Following rapid replication in the conjunctival epithelium, the herpesviruses ascend via sensory neuron axons to the trigeminal ganglia, where they establish a latent infection that persists for the cat's entire life (Andrews, 2001:9; Gaskell et al., 2007:346; Gould, 2011:334).

Stressful events are a common trigger for the reactivation of the virus in latently infected cats. Events such as moving to a new location or giving birth are known to be significant triggers for this reactivation (Gaskell et al., 2007). The virus induces mitochondrial apoptosis during its replication cycle. To counter this host defense, herpesviruses employ Latency-Associated Transcript (LAT) genes, which function to block apoptosis and thereby ensure the virus can continue to replicate (Gaskell et al., 2007:335; Maggs, 2005:97). The tegument protein VP16 is another element involved in the latency mechanism of herpesviruses. While VP16 is abundant during the initial infection of mucosal cells, its slow and inefficient transport along the axon to the neuron's nucleus is a critical factor in establishing a latent infection, as this delay prevents the immediate start of the lytic cycle (Gaskell et al., 2007:335; Maggs, 2005:97).

From a clinical standpoint, FHV-1 is a cause of upper respiratory tract infections (URTI) and, due to its cytopathic impact on epithelial cells, results in conditions like conjunctivitis or keratitis. The most common ocular problem is conjunctivitis, followed by corneal epithelial ulceration and keratitis. Conjunctivitis is characterized by conjunctival hyperemia (which may or may not be accompanied by chemosis), excessive tearing (epiphora), and signs of discomfort. Pain and swelling can cause the third eyelid to become prominent and raised. A purulent ocular discharge is produced due to the initial neutrophilic inflammatory response (Stiles, 2014: 167).

A classic and diagnostic lesion for herpesvirus is dendritic epithelial corneal ulceration. Cats suffering from FHV-1-related eye disease may also develop geographic epithelial ulcers. Both of these ulcer types can be visualized with fluorescein staining. Rose Bengal stain can also make dendritic ulcers visible, but because it is an irritant, a topical anesthetic should be applied beforehand. Keratitis can also develop without any corneal ulceration, presenting as corneal vascularization, sometimes with inflammatory cell infiltrates. Corneal disease resulting from FHV-1 is nearly always seen alongside conjunctivitis (Stiles, 2014:167).

Other corneal conditions, including corneal sequestrum and eosinophilic keratitis, have also been linked to FHV-1 (Andrews, 2001:11; Gould, 2011:337). These are more likely to develop in cases where the FHV-1-associated eye disease becomes chronic. The primary infection from FHV-1 is typically self-limiting, resolving within several weeks and leading to clinical recovery. However, a subset of cats may experience a chronic form of conjunctivitis that fails to resolve on its own. This chronic or recurring conjunctivitis can affect both eyes, though it is not unusual for it to be unilateral. This unilateral presentation can sometimes mislead a clinician into thinking that FHV-1 is not the cause (Stiles, 2014:166).

Diagnosis

The diagnosis of FHV-1 can be difficult, especially in adult cats. A patient history that includes recurrent conjunctivitis, particularly if associated with sneezing, along with a history of corneal ulcers, can strongly suggest an FHV-1 diagnosis (Maes, 2012:495830; Stiles, 2003:183). If conjunctival cytology is conducted in the early phase of the illness, a neutrophilic inflammation is the typical finding. As the condition progresses to a more chronic state, the inflammatory cell population becomes mixed, including neutrophils, lymphocytes, and plasma cells. Eosinophils and some mast cells might also be observed. It is uncommon to see intranuclear viral inclusion bodies (Maes, 2012:495830; Stiles, 2003:183).

For definitive confirmation of FHV-1, tests such as virus isolation, fluorescent antibody staining, and the Polymerase Chain Reaction (PCR) are available. Among these, PCR has emerged as the most widely used diagnostic tool. It is recommended that samples be collected from both the eyes and the oropharynx. While there can be variations between different labs, PCR is generally regarded as a highly sensitive and specific test (Maes, 2012:495830; Stiles, 2003:183).

Interpreting the results, however, demands careful judgment. A negative result does not exclude FHV-1 as the cause, and conversely, a positive result does not definitively confirm that the virus is responsible for the clinical signs. Multiple studies have demonstrated that cats with apparently normal eyes can yield positive PCR results for FHV-1 from conjunctival swabs. Despite this, a positive PCR result in a cat showing clinical signs consistent with FHV-1 allows the veterinarian to proceed with a diagnosis with a fair amount of confidence. If diagnostic tests are not an option but the clinical presentation aligns with FHV-1, a therapeutic trial with antiviral medication can be initiated, and the cat's response to the treatment can be monitored (Maes, 2012:495830; Stiles, 2003:183).

Treatment

The primary approach to treating conjunctivitis, corneal ulceration, or keratitis caused by FHV-1 should involve specific antiviral therapy. In cases where a stromal ulcer is present, there is a possibility of a secondary bacterial infection, which would require a more aggressive antibiotic treatment than what is used for a purely viral ulcer. The main purpose of using antibiotics in a viral infection is to prevent secondary bacterial infections, as the eye's defenses are compromised. Any loose epithelium should be removed via debridement with a cotton-tipped applicator. A grid keratotomy is a procedure that should be avoided in cats, as it has the potential to worsen herpesvirus-related conditions and may lead to the formation of a corneal sequestrum (La Croix et al., 2001:734). For cases with epithelial ulceration, a broad-spectrum

topical antibiotic like tobramycin is recommended. Keeping the eyes clean and regularly removing any discharge is vital for successful treatment.

The anti-herpetic medications available are detailed in Table 1. Many topical antiviral drugs are not commercially produced or are only sold in specific countries. Cidofovir, an intravenous medication for treating cytomegalovirus retinitis in humans, is a favored topical choice for cats (Thomasy and Maggs, 2016:124). When formulated as a 0.5% ophthalmic solution, cidofovir is effective against FHV-1 and remains stable for at least six months when refrigerated or frozen. It also has the benefits of not causing ocular irritation and having a long half-life, which permits twice-daily application.

Table 1: Antiviral agents used against FHV-1 infections

Generic Name	Concentration /Dose	Route of Administration	Dosing Interval (Hours)	Mechanism of Action
Cidofovir (compounded solution)	0.5%	Ophthalmic	12	Acyclic nucleoside phosphonate; inhibits viral DNA synthesis.
Trifluridine (solution)	1%	Ophthalmic	4-6	Fluorinated pyrimidine nucleoside; inhibits viral DNA synthesis.
Ganciclovir (ointment)	0.15%	Ophthalmic	4-6	Guanosine analog; inhibits viral DNA synthesis.
Idoxuridine (compounded solution)	0.1%	Ophthalmic	4-6	Thymidine analog; inhibits viral DNA synthesis.
Vidarabine (compounded ointment)	3%	Ophthalmic	4-6	Adenosine analog; inhibits viral DNA synthesis.
Acyclovir (ointment)	3%	Ophthalmic	4-6	Purine analog; inhibits viral DNA synthesis.
Famciclovir (tablet)	40 mg/kg	Oral	8	Metabolized to penciclovir, an acyclic nucleoside analog; inhibits viral polymerase and DNA synthesis.

Acyclovir is not recommended for cats as it shows poor efficacy against FHV-1, unlike its effectiveness against human herpes simplex virus (HSV). Other options like idoxuridine, trifluridine, and ganciclovir are effective but

must be applied 4-6 times a day and can cause irritation to the eye. The oral medication famciclovir (a prodrug that converts to penciclovir) is commonly used for HSV and its use in cats has grown; it is considered safe and effective for short-term use of 2-3 weeks (Thomasy et al., 2011:87). The ideal dosage, however, is still being determined. Current information indicates that a dose of 40 mg/kg three times daily may be effective, though some veterinarians report success with lower doses and less frequent administration (Thomasy et al., 2012). A study on high-dose topical recombinant human α2b and feline ω interferon for viral keratoconjunctivitis found neither interferon to be more beneficial than a placebo; thus, this treatment is not recommended (Stiles, 2014).

In some felines, especially those with chronic eye disease related to FHV-1, a topical anti-inflammatory medication may be necessary. The use of topical or systemic corticosteroids should be avoided because they carry a high risk of worsening herpetic disease. A topical nonsteroidal anti-inflammatory drug (NSAID), such as 0.1% diclofenac, can be quite beneficial, particularly when used alongside an antiviral medication. Likewise, topical 0.2% cyclosporine can offer anti-inflammatory benefits without substantially raising the risk of exacerbating the herpetic condition. For cats with chronic conjunctivitis, recovery can be slow, sometimes requiring several months of continuous treatment (Stiles et al., 2014:168).

Several triggers can lead to recurrent FHV-1 episodes in cats. These triggers include the administration of systemic or ocular corticosteroids or other immunosuppressive agents, psychological or physiological stress, pregnancy and lactation, surgery, and other concurrent health problems. For some cats, the administration of modified-live FHV-1 vaccines can even induce clinical signs of the disease. Veterinarians and owners should, whenever feasible, try to reduce these risk factors for cats known to be susceptible to herpetic disease. The outlook for resolving FHV-1-related ocular surface issues is typically moderate to good, provided the therapy is appropriate and sustained for a sufficient time, although some cats may experience relapses.

Prevention and Control

The most effective way to protect against FHV is through vaccination. Vaccination is critical because FHV-1 is a highly prevalent and easily spread virus that can lead to severe clinical outcomes (Gaskell et al., 2007: 353). Vaccines for FHV-1 have been on the market for many years. They are commercially sold as combination vaccines that also protect against Feline Coronavirus (FCoV), Feline Calicivirus (FCV), and Feline Panleukopenia virus. These are available in both modified-live and inactivated forms (Summers et al., 2017:829).

After receiving attenuated FHV-1 vaccines, there is a slight risk that the vaccine strain itself could cause an infection. Therefore, precautions should be taken to stop the cat from sniffing or licking the site of injection (Karapınar et al., 2014:16). In crowded environments like shelters and catteries, intranasal modified-live vaccines are an option. The benefit of these vaccines is that they offer quicker protection, establishing effective immunity in just 4 to 6 days (Gaskell et al., 2007: 344; Lappin et al., 2006: 160; Dawson et al., 2001:19). Inactivated vaccines are considered the safest choice in these settings because they have a minimal chance of causing a vaccine-induced infection and do not pose a risk of viral shedding. Some of these inactivated vaccines are specifically approved for pregnant queens; when given during pregnancy, they can also pass protection on to the kittens (Gaskell et al., 2007:351).

CONCLUSION

Feline Herpesvirus-1 (FHV-1) remains one of the most widespread and clinically significant viral agents affecting domestic cats worldwide. The virus's ability to establish a lifelong latent state, paired with the diverse range of eye-related problems it causes, makes it a persistent challenge for feline medicine. FHV-1 is the principal agent behind conjunctivitis, keratitis, and more severe corneal conditions like sequestra and eosinophilic keratitis, which can all severely affect a cat's vision and overall quality of life if not properly managed (Stiles, 2014:167; Gaskell et al., 2007:338).

An accurate diagnosis is crucial for providing targeted treatment. While clinical observations provide important clues, laboratory confirmation, especially through PCR, is still the most sensitive and specific way to identify an active infection (Maggs, 2005:95). Where confirmatory testing is unavailable, a diagnosis is often based on the pattern of symptoms, an approach commonly used in areas with limited resources.

Treatment plans are designed to inhibit viral replication, ease clinical signs, and avert secondary issues. Antiviral drugs like cidofovir and famciclovir have proven to be effective in clinical settings and are the primary tools for pharmacological treatment (Thomasy et al., 2012:38). Supportive measures, such as antibiotics, eye lubricants, and non-steroidal anti-inflammatory drugs, are also a critical part of the management plan.

Preventive strategies revolve around vaccination and stress management. Although vaccination does not entirely prevent infection or reactivation, it does substantially reduce the severity and length of the illness

(Scherk et al., 2013:785). In places with high cat densities, effective biosecurity protocols and prompt immunization are vital for controlling outbreaks.

To summarize, the successful management of FHV-1 requires a multifaceted approach that includes early diagnosis, treatment based on evidence, and robust preventive actions. Ongoing research into antiviral drug dynamics, vaccine effectiveness, and the mechanisms of viral latency will be essential for improving therapeutic results and achieving long-term control of the disease in feline populations.

REFERENCE

Andrew, S. E.(2001). Ocular manifestations of feline herpesvirus. *Journal of Feline Medicine and Surgery, 3*(1), 9–16.Dawson, S., Willoughby, K., Gaskell, R. M., Wood, G., ve Chalmers, W. S.(2001). A field trial to assess the effect of vaccination against feline herpesvirus, feline calicivirus and feline panleucopenia virus in 6-week-old kittens. *Journal of Feline Medicine and Surgery, 3*(1), 17-22.

Gaskell, R., Dawson, S., Radford, A., ve Thiry, E.(2007). Feline herpesvirus. *Veterinary Research, 38*(2), 337–354.

Gatherer, D., Depledge, D. P., Hartley, C. A., Szpara, M. L., Vaz, P. K., Benkő, M., Brandt, C. R., Bryant, N. A., Dastjerdi, A., Doszpoly, A., Gompels, U. A., Inoue, N., Jarosinski, K. W., Kaul, R., Lacoste, V., Norberg, P., Origgi, F. C., Orton, R. J., Pellett, P. E., Schmid, D. S., Reddy, M. K. S., Park, M.-S., Abdel-Hamid, M. N., Abdel-Rahman, A. M. G., Chinchar, V. G., Kemenesi, G., van der Sluijs, C. R. L. R., Marz, M., ve Davison, A. J.(2021). ICTV virus taxonomy profile: Herpesviridae 2021. *The Journal of General Virology, 102*(10), 001673.

Gould, D.(2011). Feline herpesvirus-1: ocular manifestations, diagnosis and treatment options. *Journal of Feline Medicine and Surgery, 13*(5), 333–346.

Grail, A., Harbour, D. A., ve Chia, W.(1991). Restriction endonuclease mapping of the genome of feline herpesvirus type 1. *Archives of Virology, 116*, 209–220.

Heldwein, E. E. ve Krummenacher, C.(2008). Entry of herpesviruses into mammalian cells. *Cellular and Molecular Life Sciences, 65*(11), 1653–1668.

Johnson, L. R. ve Maggs, D. J.(2005). Feline herpesvirus type-1 transcription is associated with increased nasal cytokine gene transcription in cats. *Veterinary Microbiology, 108*(3-4), 225–233.

Karapınar, Z., Dinçer, E., Ataseven, S. V., ve Karaca, M.(2014). Felid herpesvirus-1 infection in Van cats with conjunctivitis. *Van Veterinary Journal, 25*, 15–17.

La Croix, N. C., van der Woerdt, A., ve Olivero, D. K.(2001). Nonhealing corneal ulcers in cats: 29 cases (1991-1999). *Journal of the American Veterinary Medical Association, 218*(5), 733–735.

Lappin, M. R., Sebring, R. W., Porter, M., Radecki, S. J., ve Veir, J.(2006). Effects of a single dose of an intranasal feline herpesvirus 1, calicivirus, and panleukopenia vaccine on clinical signs and virus shedding after challenge with virulent feline herpesvirus 1. *Journal of Feline Medicine and Surgery, 8*(3), 158-163.

Maeda, K., Yokoyama, N., Fujita, K., Maejima, M., ve Mikami, T.(1997). Heparin-binding activity of feline herpesvirus type 1 glycoproteins. *Virus Research, 52*(2), 169–176.

Maes, R.(2012). Felid herpesvirus type 1 infection in cats: a natural host model for alphaherpesvirus pathogenesis. *ISRN Veterinary Science, 2012*, 495830.

Maggs, D. J.(2005). Update on pathogenesis, diagnosis, and treatment of feline herpesvirus type 1. *Clinical Techniques in Small Animal Practice, 20*, 94-101.

Mettenleiter, T. C.(2004). Budding events in herpesvirus morphogenesis. *Virus Research, 106*(2), 167–180.

Mijnes, J. D., Lutters, B. C., Vlot, A. C., van Anken, E., Horzinek, M. C., Rottier, P. J., ve de Groot, R. J.(1997). Structure-function analysis of the gE-gI complex of feline herpesvirus: mapping of gI domains required for gE-gI interaction, intracellular transport, and cell-to-cell spread. *Journal of Virology, 71*(11), 8397–8404.

Rota, P. A., Maes, R. K., ve Evermann, J. F.(1986). Biochemical and antigenic characterization of feline herpesvirus-1-like isolates from dogs. *Archives of Virology, 89*(1-4), 57–68.

Scherk, M. A., Ford, R. B., Gaskell, R. M., Hartmann, K., Hurley, K. F., Lappin, M. R., Levy, J. K., Little, S. E., Nordone, S. K., ve Sparkes, A. H.(2013). 2013 AAFP feline vaccination advisory panel report. *Journal of Feline Medicine and Surgery, 15*(9), 785-808.

Stiles, J.(2003). Feline herpesvirus. *Clinical Techniques in Small Animal Practice, 18*(3), 178–185.

Stiles, J.(2014). Ocular manifestations of feline viral diseases. *The Veterinary Journal, 201*(2), 166–173.

Summers, S. C., Ruch-Gallie, R., Hawley, J. R., ve Lappin, M. R.(2017). Effect of modified live or inactivated feline herpesvirus-1 parenteral vaccines on clinical and laboratory findings following viral challenge. *Journal of Feline Medicine and Surgery, 19*(8), 824-830.

Thomasy, S. M., Lim, C. C., Reilly, C. M., Kass, P. H., Lappin, M. R., ve Maggs, D. J.(2011). Evaluation of orally administered famciclovir in cats experimentally infected with feline herpesvirus type-1. *American Journal of Veterinary Research, 72*(1), 85–95.

Thomasy, S. M., Covert, J. C., Stanley, S. D., ve Maggs, D. J.(2012). Pharmacokinetics of famciclovir and penciclovir in tears following oral administration of famciclovir to cats: a pilot study. *Veterinary Ophthalmology, 15*(5), 299-306.

Thomasy, S. M. ve Maggs, D. J.(2016). A review of antiviral drugs and other compounds with activity against feline herpesvirus type 1. *Veterinary Ophthalmology, 19*(Suppl 1), 119–130.

Lower Extremity Joints and Clinical Anatomy

Albaraa RIYADH MOHAMMED AL-SAMANEE [1]
Zülal ÖNER [2]

Dr. Albaraa RIYADH MOHAMMED AL-SAMANEE
Karabuk University, Faculty of Medicine, Department of Anatomy, dr.mousl.love@gmail.com, 0000-0002-6707-4085
Prof. Dr. Zülal EKINCIOĞLU ÖNER
İzmir Bakırçay University, Faculty of Medicine, Department of Anatomy, zulal.oner@bakircay.edu.tr, 0000-0003-0459-1015

ABSTRACT

This chapter comprehensively examines the anatomy, biomechanics, and clinical pathologies of the lower extremity joints, emphasizing their critical roles in mobility, weight-bearing, and balance. The hip joint a ball-and-socket structure stabilized by the acetabulum and ligaments (iliofemoral, pubofemoral) is susceptible to osteoarthritis, fractures, femoroacetabular impingement (FAI), and avascular necrosis. Management ranges from conservative therapies to surgical interventions like hip arthroplasty. The knee joint, a hinge mechanism reinforced by cruciate ligaments and menisci, commonly suffers from osteoarthritis, ACL/meniscal injuries, and patellofemoral pain syndrome, addressed via physical therapy, bracing, or joint replacement. The ankle joint (talocrural articulation), stabilized by collateral ligaments, frequently incurs sprains, Achilles tendon injuries, and fractures, with chronic instability requiring proprioceptive rehabilitation or ligament repair. Foot joints (subtalar, metatarsophalangeal) enable complex motions but are prone to plantar fasciitis, hallux valgus, Morton's neuroma, and stress fractures. Systemic conditions like gout and inflammatory arthritis also impact these joints. Diagnostic approaches integrate clinical tests (e.g., Lachman test for ACL tears) and advanced imaging (MRI, radiography). Treatment strategies prioritize anatomy-informed interventions: NSAIDs, orthotics, and corticosteroid injections for mild cases, progressing to arthroscopic surgery or joint replacement for advanced pathologies. Understanding the intricate anatomy and biomechanics of these joints remains foundational for accurate diagnosis and effective management of lower extremity disorders.

Keywords: *Lower Extremity Joints, Hip Joint Anatomy, Knee Ligament Injuries, Ankle Sprains And Fractures, Foot Joint Disorders, Osteoarthritis, Clinical Anatomy.*

INTRODUCTION

Several important joints that are necessary for mobility, weight-bearing, and balance maintenance define the lower extremity (Moore et al., 2018). Included among these joints are the hip, knee, ankle, and several foot joints. Every joint is carefully engineered to give stability and flexibility, which helps to enable complicated motions required for standing, running, and walking (Gray, 2016). Diagnosing and treating musculoskeletal diseases depend on an awareness of the architecture of these joints as well as their clinical relevance. Clinically, the hip joint is prone to osteoarthritis, fractures, and labral tears; in severe situations, typically procedures including hip replacement are necessary (Katz et al., 2021; Parker & Johansen, 2006). Commonly afflicted by ligament injuries, meniscal tears, patellofemoral pain syndrome, and

osteoarthritis, the knee joint causes discomfort and functional restrictions (Georgiev & Angelov, 2019). Sprains, fractures, tendonitis, and arthritis can all affect the ankle joint;
ankle sprains are especially prevalent in sports (Sarcon et al., 2019). Often causing pain and trouble with walking, foot joints---especially the subtalar and metatarsophalangeal joints---can develop disorders including bunions, flat feet, plantar fasciitis, and hammertoe (Riddle et al., 2003; Cai et al., 2023). Good control of these disorders calls for a comprehensive knowledge of joint anatomy and appropriate clinical examination for correct diagnosis and therapy planning.

HIP JOINT

Connecting the femur (thigh bone) to the pelvis, the hip joint is a ball-and-socket junction (Moore et al., 2018). Flexion, extension, abduction, adduction, and rotation are among the extensive range of motion made possible here. Mobility and weight-bearing depend on this one joint. The acetabulum, a deep pelvis socket, and the strong ligaments surrounding it including the iliofemoral and pubofemoral ligaments help to mostly determine the stability of the joint (Gray, 2016). Clinically, developmental dysplasia, fractures, and arthritis most often impact the hip joint and can cause reduced mobility and pain (Kokavec & Bialik, 2007).

Clinical Considerations of the Hip Joint

Osteoarthritis of the Hip: A degenerative disorder causing increasing cartilage loss, discomfort, stiffness, and limited range of motion, osteoarthritis of the hip is among the risk factors are aging, obesity, past joint damage, and hereditary tendency (Katz et al., 2021). Treatment consists of non-steroidal anti-inflammatory drugs (NSAIDs), physical therapy, weight control, and in severe cases, complete hip replacement.

Hip Fractures: Common in older people from falls and osteoporosis, hip fractures are usually they include the subtrochanteric, intertrochanteric, or femoral neck areas (Parker & Johansen, 2006). Often requiring surgical intervention, including internal fixation or hip arthroplasty, hip fractures are linked with great morbidity and death.

Femoroacetabular Impingement (FAI): Results from aberrant bone development that causes impingement between the femoral head and acetabulum, therefore producing pain and limited movement (Kaplan et al.,

2010). It might cause early-onset osteoarthritis. Treatment consists in physical therapy, activity modification, and, if needed, surgical correction.

Developmental Dysplasia of the Hip: A congenital disorder results from improper fit of the femoral head into the acetabulum (Kokavec & Bialik, 2007). Management with bracing or surgical correction depends on early identification in order to prevent long-term joint deterioration and instability.

Avascular Necrosis of the Hip: Sometimes referred to as osteonecrosis or ischemic necrosis, results from loss of blood flow to the femoral head, therefore causing death of bone structure (Konarski et al., 2022). Left untreated, it may lead to hip joint arthritis and finally the femoral head's collapse. Among the risk factors are trauma, alcohol usage, corticosteroid use, and sickle cell disease. From basic decompression in early stages to complete hip arthroplasty in advanced situations, treatment choices span.

Hip Labral Tears: Usually resulting from trauma, repeated motions, or structural anomalies like FAI, hip labral tears damage the acetabular labrum (Su et al., 2019). Among the symptoms include clicking, discomfort, and instability. Magnetic Resonance Imaging (MRI) confirms diagnosis; treatment calls for either physical therapy, intra-articular injections, or arthroscopic repair.

Trochanteric Bursitis: Often brought on by either direct trauma, muscular imbalances, or repeated stress, trochanteric bursitis is inflammation of the trochanteric bursa producing lateral hip pain (Speers & Bhogal, 2017). NSAIDs, physical therapy, corticosteroid injections, and activity modification all part of management.

Snapping Hip Syndrome: Characterized by an audible cracking or popping feeling around the hip joint brought on by tendon movement over bone surfaces, cracking Hip Syndrome it's rather typical of dancers and athletes (Musick & Varacallo, 2023). Treatment consists in stretching, strengthening exercises, and in cases of persistent development surgical surgery.

Hip Dislocations: Usually stemming from high-energy trauma such motor vehicle accidents, hip dislocations usually posterior dislocations, they might cause avascular necrosis and sciatic nerve damage (Clegg et al., 2010). Minimizing problems depends on quick reduction and rehabilitation.

KNEE JOINT

With the patella (kneecap) seated in front of the knee joint to guard it and facilitate mobility, this hinge joint links the femur to the tibia (Bozkurt & Açar, 2021). Walking, running, and jumping all depend on the knee; its action is essentially flexion and extension. When the knee is flexed, though, it also lets for small rotational motions (Chmielewski et al., 2002). Different ligaments, including the anterior cruciate ligament (ACL) and the posterior cruciate ligament, help to keep the joint stable; also, the menisci cushion between the femur and tibia. Common among sportsmen, knee injuries especially ACL rips and meniscal injuries can seriously limit function (Gelber et al., 2022).

Clinical Considerations of the Knee Joint

Osteoarthritis: A degenerative joint disease marked by cartilage breakdown, osteoarthritis (OA) causes pain, stiffness, and functional disability (Georgiev & Angelov, 2019). Among the risk factors are aging, obesity, past joint injuries, and genetic inclination. Management calls for physical therapy, weight loss, NSAIDs, and surgical choices including total knee replacement in extreme cases.

Anterior Cruciate Ligament Injuries: Common in athletes, particularly in sports demanding turning, rapid stops, and jumps, ACL injuries raise a risk of subsequent meniscal injury and cause knee instability (Chmielewski et al., 2002). MRI and a Lachman test help to confirm diagnosis. Therapies available are surgical repair or rehabilitation.

Meniscal Tears: Meniscal tears can arise from either degenerative changes or acute trauma (Gelber et al., 2022). Among the symptoms include locking, clicking, swelling, and pain. Diagnosis calls an MRI and a clinical assessment using Murray's test. Treatment can call for arthroscopic meniscectomy/repair or physical therapy.

Patellofemoral Pain Syndrome: Often referred to as runner's knee, Patellofemoral Pain Syndrome causes anterior knee pain particularly with stair climbing or extended sitting (Singerman et al., 1995). Often it results from overuse, patellar maltracking, or muscular imbalances. Management calls for taping, strengthening exercises (quadriceps and hip abductors), and orthotics.

Bursitis: Trauma or repeated friction causes inflammation of the bursae e.g., prepatellar, pes anserine (Bozkurt & Açar, 2021). Presents localized swelling and discomfort. In chronic cases, treatment consists in rest, ice, NSAIDs, and corticosteroid injections.

Avascular Necrosis: Is the loss of blood flow to the femoral condyles that results in bone death (Bell et al., 2024). Trauma, alcohol and corticosteroid usage are among the risk factors. The preferred diagnosis instrument is MRI. Treatment spans conservative care to surgical procedures including knee replacements or core decompression.

Knee Fractures and Dislocations: Patellar fractures and tibial plateau fractures, which follow from high-impact trauma, call for either surgical treatment or immobilization (Bozkurt & Açar, 2021). Knee dislocations are orthopedic crises brought on by neurovascular damage that is, damage to the popliteal artery. Crucially important are quick reduction and vascular evaluation.

Gout and Inflammatory Arthritis: Conditions including gout, rheumatoid arthritis, and septic arthritis can commonly affect the knee (Asghari et al., 2024). Urate crystal deposition causes acute, very painful swelling in gout. Rheumatoid arthritis causes joint degeneration, synovial enlargement, and persistent inflammation. Treatment ranges from NSAIDs and colchicine (for gout) to Disease-Modifying Antirheumatic Drugs (DMARDs) (for rheumatoid arthritis).

ANKLE JOINT

Comprising a hinge joint between the tibia and fibula and the talus bone of the foot, the ankle joint also called the talocrural joint is walking and running requires dorsiflexion and plantar flexion, which this joint lets occur (Golanó et al., 2014). Several ligaments including the lateral collateral ligaments and the deltoid ligament on the medial side help to keep the ankle stable (Sarcon et al., 2019). Particularly in sportsmen and people with high degrees of physical activity, ankle sprains especially those involving the lateral ligaments are among the most frequent injuries.

Clinical Considerations of the Ankle Joint

Ankle Sprains: One of the most frequent musculoskeletal injuries, ankle sprains usually affect the lateral ligament complex especially the anterior talofibular ligament result from too inversion of the foot (Sarcon et al., 2019). To stop chronic instability, treatment consists in rest, ice, compression, elevation, bracing, and rehabilitation.

Achilles Tendon Injuries: The Achilles tendon is prone to tendinitis, tendinosis, and rupture (Järvinen et al., 2005). Achilles tendinopathy which causes discomfort and stiffness at the posterior ankle can be brought on by overuse, inappropriate shoes, and abrupt increases in activity. Usually linked with a sudden popping feeling, complete ruptures need for either conservative or surgical treatment.

Fractures of the Ankle: Commonly resulting from high-impact trauma or twisting injuries, fractures of the ankle include bimalleolar, trimalleolar, and medially, lateral, or posterior malleolar fractures (Glazebrook et al., 2021). While displaced fractures usually call for surgical fixation, stable fractures may be handled with immobilization.

Tarsal Tunnel Syndrome: Compression of the tibial nerve as it traverses the tarsal tunnel causes tarsal tunnel syndrome (Fujihara, 2021). Along the medial side of the foot, symptoms consist in burning pain, tingling, and numbness. Tinel's test and nerve conduction investigations confirm diagnosis. Management calls for orthoses, corticosteroid injections, and, in severe situations, surgical decompression.

Plantar Fasciitis: Especially in the morning or after extended standing, plantar fasciitis inflammation of the plantar fascia at its origin on the calcaneus causes heel pain (Riddle et al., 2003). Among the risk factors are misuse, obesity, and too strong foot pronation. In situations of refractory, treatment comprises of stretching exercises, orthotics, NSAIDs, and corticosteroid injections.

Osteoarthritis of the Ankle: Less prevalent than knee or hip osteoarthritis, osteoarthritis of the ankle usually originates from post-traumatic changes causing pain, stiffness, and limited joint movement (Bloch et al., 2015). While severe instances may need ankle fusion or total ankle replacement, conservative treatment consists in physical therapy, bracing, and NSAIDs.

Chronic Ankle Instability: Results of repeated ankle sprains causing mechanical and functional instability are known as chronic ankle instability (do Amaral E Castro et al., 2023). Patients suffer from ongoing discomfort and regular occurrences of giving way. Management calls for physical therapy emphasizing proprioception, strengthening exercises, and in severe cases surgical ligament restoration.

Gout and Inflammatory Arthritis: including rheumatoid arthritis and other inflammatory arthropathies, commonly affect the ankle (Busso, 2010). Because of urate crystal formation, gout shows with sudden, acute pain, warmth, and swelling. Management calls for lifestyle changes, colchicine,

and NSAIDs. Progressive joint damage brought on by rheumatoid arthritis may call for DMARDs or biologic treatments.

FOOT JOINTS

Among the various minor joints in the foot are the metatarsophalangeal joints, the midtarsal joint, and the subtalar joint (Netter, 2018). These joints enable appropriate gait mechanics and balance, therefore contributing to the complex motions of the foot including inversion, eversion, and toe flexion (Riddle et al., 2003). Understanding foot joint anatomy is crucial for proper treatment since clinical disorders including flat feet, bunions, and arthritis can seriously compromise foot function and generate discomfort.

Clinical Considerations of the Foot Joints

Plantar Fasciitis: Common cause of heel discomfort, plantar fasciitis results from inflammation of the plantar fascia at its connection to the calcaneus (Ali et al., 2024). It links to obesity, too much foot pronation, and extended standing. Many times, patients wake up or after rest in great discomfort. For refractory instances, management calls for stretches, orthotics, NSAIDs, and corticosteroid injections.

Hallux Valgus (Bunion): A deformity marked by lateral displacement of the great toe and medial protrusion of the first metatarsal head is hallux valgus, or bunion (Cai et al., 2023). It is sometimes linked to ill-fitting shoes and genetic inclination. Among the symptoms include discomfort, swelling, and shoe-wear problems. Treatment spans from surgical correction in extreme situations to footwear modification and orthotics.

Metatarsalgia: Often brought on by high-impact sports, incorrect footwear, or foot abnormalities, metatarsalgia pain in the ball of the foot is caused by too strong pressure on the metatarsal heads (Cooke et al., 2021). Management consists in NSAIDs, cushioned insoles, and activity adjustment.

Morton's Neuroma: Most usually between the third and fourth metatarsals, Morton's Neuroma is a painful disorder brought on by thickening of the interdigital nerve (Biz et al., 2024). Patients claim toe burning pain, tingling, and numbness. In situations of persistent disease, treatment consists in corticosteroid injections, shoe modification, and surgical excision.

Tarsal Coalition: A congenital disorder known as tarsal coalition causes aberrant bony, cartilaginous, or fibrous connections between tarsal bones to cause stiffness and pain in adolescence (Saxena et al., 2022). Radiographic imaging confirms the diagnosis. Treatment consists in NSAIDs, orthotics, and occasionally surgical resection.

Osteoarthritis of the Foot Joints: A degenerative joint disease impacting the tarsometatarsal, subtalar, and metatarsophalangeal joints, osteoarthritis of the foot joints causes pain, stiffness, and reduced mobility (Priftakis, 2023). Risk factors consist in obesity, trauma, and aging. Treatment consists in NSAIDs, orthotic support, and in severe cases joint fusion or replacement.

Stress Fractures: Common in athletes and those engaged in repeated high-impact activities, stress fractures develop from overuse and inadequate bone repair (Miller & Kaeding, 2015). The metatarsals are usually impacted. Bone scans or MRI help to confirm diagnosis. Management consists in activity modification, immobilization, and calcium/vitamin D optimization.

Diabetic Foot Complications: Patients with diabetes run a risk of neuropathic ulcers, Charcot arthropathy, and infections brought on by peripheral neuropathy and inadequate circulation (Stancu et al., 2023). Correct foot care, diabetes control, and frequent doctor visits constitute part of prevention. Treatment could call for debridement, antibiotics, and in severe circumstances amputation.

REFERENCES

Moore, Keith L., Arthur F. Dalley, and Anne M. R. Agur. *Clinically Oriented Anatomy.* 8th ed. Philadelphia: Wolters Kluwer, 2018.

Gray, Henry. *Gray's Anatomy: The Anatomical Basis of Clinical Practice.* 41st ed. Edinburgh: Elsevier Churchill Livingstone, 2016.

Golanó, P., Dalmau-Pastor, M., Vega, J., & Batista, J. P. (2014). The Ankle in Football (pp. 1–24). Springer, Milan. ISBN: 978-2-8178-0522-1

Netter, Frank H. *Atlas of Human Anatomy.* 7th ed. Philadelphia: Elsevier, 2018.

Katz, J. N., Arant, K. R., & Loeser, R. F. (2021). Diagnosis and Treatment of Hip and Knee Osteoarthritis: A Review. *JAMA*, *325*(6), 568–578.

Parker, M., & Johansen, A. (2006). Hip fracture. BMJ (Clinical research ed.), 333(7557), 27–30.

Kaplan, K. M., Shah, M. R., & Youm, T. (2010). Femoroacetabular impingement--diagnosis and treatment. Bulletin of the NYU hospital for joint diseases, 68(2), 70–75.

Kokavec, M., & Bialik, V. (2007). Developmental dysplasia of the hip. Prevention and real incidence. Bratislavske lekarske listy, 108(6), 251–254.
Konarski, W., Poboży, T., Śliwczyński, A., Kotela, I., Krakowiak, J., Hordowicz, M., & Kotela, A. (2022). Avascular Necrosis of Femoral Head-Overview and Current State of the Art. International journal of environmental research and public health, 19(12), 7348.
Su, T., Chen, G. X., & Yang, L. (2019). Diagnosis and treatment of labral tear. Chinese medical journal, 132(2), 211–219.
Speers, C. J., & Bhogal, G. S. (2017). Greater trochanteric pain syndrome: a review of diagnosis and management in general practice. The British journal of general practice: the journal of the Royal College of General Practitioners, 67(663), 479–480.
Musick, S. R., & Varacallo, M. A. (2023). Snapping Hip Syndrome. In StatPearls. StatPearls Publishing.
Clegg, T. E., Roberts, C. S., Greene, J. W., & Prather, B. A. (2010). Hip dislocations--epidemiology, treatment, and outcomes. Injury, 41(4), 329–334.
Georgiev, T., & Angelov, A. K. (2019). Modifiable risk factors in knee osteoarthritis. Rheumatology International, 39(7), 1145-1157.
Chmielewski, T. L., Rudolph, K. S., & Snyder-Mackler, L. (2002). Development of dynamic knee stability after acute ACL injury. Journal of electromyography and kinesiology: official journal of the International Society of Electrophysiological Kinesiology, 12(4), 267–274.
Gelber, P. E., Ramírez-Bermejo, E., & Fariñas, O. (2022). Early Postoperative CT Scan Provides Prognostic Data on Clinical Outcomes of Fresh Osteochondral Transplantation of the Knee. The American journal of sports medicine, 50(14), 3812–3818.
Singerman, R., White, C., & Davy, D. T. (1995). Reduction of patellofemoral contact forces following anterior displacement of the tibial tubercle. Journal of orthopaedic research: official publication of the Orthopaedic Research Society, 13(2), 279–285.
Bell, C., Feizi, A., Roytman, G. R., Ramji, A. F., Tommasini, S. M., & Wiznia, D. H. (2024). Fabricating patient-specific 3D printed drill guides to treat femoral head avascular necrosis. 3D printing in medicine, 10(1), 10.
Bozkurt, M., & Açar, H. İ. (Eds.). (2021). Clinical Anatomy of the Knee: An Atlas. Springer.
Asghari, K.M., Zahmatyar, M., Seyedi, F. et al. Gout: global epidemiology, risk factors, comorbidities and complications: a narrative review. BMC Musculoskelet Disord 25, 1047 (2024).
Sarcon, A. K., Heyrani, N., Giza, E., & Kreulen, C. (2019). Lateral Ankle Sprain and Chronic Ankle Instability. Foot & ankle orthopaedics, 4(2), 2473011419846938.
Järvinen, T. A., Kannus, P., Maffulli, N., & Khan, K. M. (2005). Achilles tendon disorders: etiology and epidemiology. Foot and ankle clinics, 10(2), 255–266.
Glazebrook, M., Burgesson, B. N., Younger, A. S., & Daniels, T. R. (2021). Clinical outcome results of total ankle replacement and ankle arthrodesis: a pilot randomised controlled trial. Foot and ankle surgery: official journal of the European Society of Foot and Ankle Surgeons, 27(3), 326–331.
Fujihara, F. (2021). Tarsal Tunnel Syndrome. In: Isu, T., Kim, K. (eds) Entrapment Neuropathy of the Lumbar Spine and Lower Limbs. Springer, Singapore.

Ali, Q., Long, Y. & Ali, M. Prevalence, causes, and treatment of plantar fasciitis in young females of a medical college. Bull Fac Phys Ther 29, 31 (2024).

Bloch, B., Srinivasan, S., & Mangwani, J. (2015). Current Concepts in the Management of Ankle Osteoarthritis: A Systematic Review. The Journal of foot and ankle surgery: official publication of the American College of Foot and Ankle Surgeons, 54(5), 932–939.

do Amaral E Castro, A., Godoy-Santos, A. L., & Taneja, A. K. (2023). Advanced Imaging in the Chronic Lateral Ankle Instability: An Algorithmic Approach. Foot and ankle clinics, 28(2), 265–282.

Busso, N., So, A. Gout. Mechanisms of inflammation in gout. Arthritis Res Ther 12, 206 (2010).

Riddle, D. L., Pulisic, M., Pidcoe, P., & Johnson, R. E. (2003). Risk factors for Plantar fasciitis: a matched case-control study. The Journal of bone and joint surgery. American volume, 85(5), 872–877.

Cai, Y., Song, Y., He, M. et al. Global prevalence and incidence of hallux valgus: a systematic review and meta-analysis. J Foot Ankle Res 16, 63 (2023).

Cooke, R., Manning, C., Palihawadana, D., Zubairy, A. I., & Khan, S. H. (2021). Metatarsalgia: anatomy, pathology and management. British journal of hospital medicine (London, England : 2005), 82(9), 1–8.

Biz, C., Crimì, A., Mori, F. et al. Morton's neuroma: who, when and how contributed to its description and treatment?. International Orthopaedics (SICOT) (2024).

Saxena, A., Allen, R., Wright, A. et al. Tarsal coalition resections: a long-term retrospective analysis of 97 resections in 78 patients. J Orthop Surg Res 17, 458 (2022).

Priftakis, D. (2023). Osteoarthritis of the Foot and Ankle. In: Van den Wyngaert, T., Gnanasegaran, G., Strobel, K. (eds) Clinical Atlas of Bone SPECT/CT. Springer, Cham.

Miller, T.L. & Kaeding, C.C.. (2015). Stress Fractures in Athletes: Diagnosis and Management. 10.1007/978-3-319-09238-6.

Stancu, B., Ilyés, T., Farcas, M., Coman, H. F., Chiș, B. A., & Andercou, O. A. (2023). Diabetic Foot Complications: A Retrospective Cohort Study. International Journal of Environmental Research and Public Health, 20(1), 187.

A Narrative Review on the Effect of Therapeutic Taping on Upper Extremity Functional Status in Patients with Ischemic Stroke

Mehmet SÖNMEZ[1]

1- Asst. Prof. Dr., Mehmet SÖNMEZ, Department of Orthopedical Rehabilitation, Erzurum Technical University Health Science Faculty, Physiotherapy and Rehabilitation, mehmet.sonmez@erzurum.edu.tr, ORCID: 0000-0002-3617-9087 Tel:444-5-388-(2739)

ABSTRACT

Purpose: This review aims to comprehensively evaluate the existing literature on the effects of therapeutic taping, specifically kinesiology taping, on upper extremity function in patients with ischemic stroke. It seeks to synthesize the current evidence to inform clinical practice and identify knowledge gaps in this field.

Approach: A narrative review methodology was employed to analyze the effects of therapeutic taping. The document synthesizes findings on various mechanisms of action, including proprioceptive feedback, muscle activation/inhibition, edema reduction, pain management, and subluxation management. It also compares the results of different application protocols and their impact on motor function, spasticity, and shoulder pain.

Key Results: The review found that therapeutic taping is particularly effective in reducing shoulder subluxation and post-stroke shoulder pain, with consistent evidence supporting its use for these conditions. The results regarding its direct effects on spasticity and overall motor function are more mixed and sometimes conflicting, indicating that the efficacy depends on the specific taping technique, application duration, and patient characteristics.

Conclusion: Therapeutic taping serves as a valuable complementary intervention within a comprehensive rehabilitation program for stroke survivors. It is not a stand-alone solution but can contribute significantly to improving upper extremity function, especially for pain and subluxation. Future research should focus on standardizing application protocols and conducting long-term studies to better understand its effectiveness.

Keywords: Stroke, Kinesiology Taping, Upper Extremity, Rehabilitation, Hemiplegia, Spasticity, Shoulder Pain.

INTRODUCTION

Stroke constitutes a significant global health problem, representing the foremost cause of permanent disability and mortality among adults. According to data from the World Health Organization (WHO), approximately 15 million people suffer a stroke each year, and one-third of these individuals are left with permanent disabilities. (Feigin et al., 2025) The incidence of stroke increases with age, and it has been determined that approximately 87% of all stroke cases are of the ischemic type. Ischemic stroke is characterised by neurological deficits resulting from insufficient blood flow to the brain, with the potential to cause a wide range of motor, sensory, cognitive, and speech impairments, depending on the affected

area.(Shiber et al., 2010) Among these functional impairments, upper extremity dysfunction is one of the most common and severely debilitating issues, affecting approximately 80% of stroke patients.(Bustamante et al., 2016) The loss of upper extremity function can have a significant impact on patients' independence and social participation, particularly due to the critical role of the hand and arm in daily living activities (such as eating, dressing, and personal hygiene). (Bustamante et al., 2016)This is one of the most significant challenges patients face during the rehabilitation process, and optimising upper extremity function is of paramount importance for regaining independent living skills and reintegrating into society. Consequently, there is a critical need for research to identify effective rehabilitation strategies that can enhance upper extremity function after stroke, with existing evidence being synthesised to inform clinical practice and improve patient outcomes.

In addition to traditional physical therapy approaches in post-stroke rehabilitation, various complementary and alternative therapies have also gained popularity in recent years. One such therapy is therapeutic taping, also known as kinesiology taping or kinesio taping. Kinesiology taping was first developed in the 1970s by Japanese chiropractor Dr. Kenzo Kase and was initially used in the rehabilitation of sports injuries.(Mostafavifar et al., 2012) The tapes are designed to have properties similar to the elasticity of human skin, and they work by lifting the skin in the applied area to create more space in the subcutaneous tissue. This mechanism is explained by physiological effects such as increasing blood and lymph circulation to reduce edema, alleviating pressure on pain receptors, facilitating or inhibiting muscle activity, enhancing proprioceptive feedback, and supporting joint stability.(Cai et al., 2016) The utilisation of therapeutic taping has become pervasive in the management of both acute and chronic musculoskeletal disorders, owing to its non-invasive, straightforward application and comparatively low financial outlay. In the domain of stroke rehabilitation, the potential of this approach has garnered the attention of researchers and clinicians. Its notable benefits include the management of spasticity, the prevention of joint subluxation(Huang et al., 2017), the augmentation of muscle activation, and the enhancement of movement control.(Wang et al., 2022)

The primary objective of this review is to comprehensively summarize and evaluate the existing literature examining the effect of therapeutic taping on upper extremity functional status in patients with ischemic stroke. Upper extremity functional recovery in stroke rehabilitation is one of the primary goals that directly impacts patients' quality of life. A systematic synthesis of existing evidence will elucidate the potential benefits, mechanisms of action, and application variability of therapeutic taping in this context. The review aims to identify knowledge gaps in this field by analyzing the effects of different taping techniques (e.g., muscle

support, ligament support, lymphatic drainage) and application durations on upper extremity motor control, muscle strength, spasticity, shoulder pain, and subluxation.

The rationale for this review stems from the need to provide a clear and up-to-date evidence base regarding the clinical efficacy of therapeutic taping in the management of upper extremity dysfunction following ischemic stroke. While therapeutic taping applications are becoming increasingly common in clinical practice, there is limited compiled and synthesized information regarding their specific effects on upper extremity function in the stroke population. This situation may cause difficulties for clinicians in evidence-based decision-making processes. Bringing together the current scattered literature and evaluating it from a critical perspective will provide practical insights for physical therapists and rehabilitation physicians regarding the integration of therapeutic taping into upper extremity rehabilitation programs after stroke. Additionally, the review will contribute to the design of future randomized controlled trials by informing hypotheses about which specific taping techniques may be more effective in which patient groups and over which time periods. This will lay the groundwork for the development of more targeted and effective intervention strategies in the field of stroke rehabilitation.

LITERATURE REVIEW

Mechanisms of Action of Therapeutic Taping

Therapeutic taping, principally kinesiology taping (KT), is a prevalent method in upper extremity rehabilitation following stroke, theorised to facilitate functional enhancement through multiple mechanisms of action. The triggering of varied physiological responses by these mechanisms is contingent on the elasticity of the tape, the tension applied, and the direction of placement. The mechanical interactions created by applying the tape to the skin have been shown to affect neurophysiological and hydrodynamic processes, leading to changes in pain, oedema, muscle activity, and proprioception.

Proprioceptive Feedback

One of the most significant problems observed in the upper extremity after stroke is the impairment of sensory information from the affected limb, particularly proprioceptive feedback. Proprioception is a sense that transmits information such as joint position, movement speed, and muscle tension to the central nervous system, and is vital for motor control and coordination.(Tuthill & Azim, 2018) Therapeutic taping increases

sensory input by stimulating mechanoreceptors (Merkel discs, Ruffini corpuscles, Pacini corpuscles) under the skin when applied to the skin. The slight pulling and pressure sensation created by the tape provides continuous feedback about joint position and movement, helping the patient better perceive the spatial location of the affected limb.(Tuthill & Azim, 2018) This increased proprioceptive input can optimize motor planning and execution in the central nervous system, thereby improving movement accuracy and coordination. For example, a taping band applied around the shoulder joint can help stabilize the joint through active muscle contractions by allowing the patient to better sense subluxation or unwanted movements of the shoulder joint.(Yim & Kim, 2024) This mechanism provides an important sensory cue for the patient to perform motor tasks more effectively, especially in situations where visual feedback is insufficient or distractions are high. Increased proprioceptive input can also accelerate motor learning processes and contribute to the reprogramming of movement patterns. (Castaño et al., 2020)

Muscle Activation/Inhibition

The effect of therapeutic taping on muscle activity is explained by the fact that it provides facilitation (activation) or inhibition (relaxation) depending on the direction of application and the amount of tension applied to the tape. When the tape is applied in the direction of the muscle fibers and stretched from the origin to the insertion of the muscle, it can trigger the muscle's stretch reflex, leading to an increase in muscle activity. This facilitative effect can help weaken or paretic muscles to strengthen and contract more effectively. For example, in a patient with deltoid muscle weakness following a stroke, a facilitative taping technique applied to the deltoid may support shoulder elevation. Conversely, when applied perpendicular to the muscle fibers or stretched from the muscle's insertion to its origin, the tape may reduce tension on the muscle and potentially decrease muscle overactivity, thereby exhibiting a spasticity-reducing or muscle-relaxing effect.(Cai et al., 2016) This inhibitory effect may help reduce muscle tone, particularly in flexor spasticity commonly seen after stroke (e.g., biceps brachii or flexor carpi ulnaris).(Karadag-Saygi et al., 2010) This mechanism of action may be related to the tape lifting the skin, reducing pressure on the subcutaneous tissues, and modulating mechanical tension on muscle receptors.(Huang et al., 2017) However, exactly how these mechanisms work and which effect is more dominant in which situations is still a matter of research and may vary between different patients.

Edema Reduction and Circulation

Following a stroke, edema development is a common complication in the upper extremities, particularly in the hemiplegic arm. This is due to impaired lymphatic drainage and slowed venous return. This edema can lead to pain, restricted joint mobility and further functional impairment.(Bell &

Muller, 2013) Therapeutic taping involves applying tape to the skin using a special 'fan' or 'lymphatic' technique to create ripples (convulsions) in the skin and form a space between the skin and subcutaneous tissues. This space facilitates the movement of lymph and interstitial fluids. The tape's lifting effect reduces pressure on lymph capillaries and increases lymph flow, helping to mobilise and reduce edema. It is also believed that the tape increases blood circulation in the applied area, thereby improving tissue nutrition. Increased microcirculation may support tissue repair and contribute to the resolution of edema. (Anvar, 2024) In stroke patients with hand and wrist edema, it has been reported that the tape directs edema from distal to proximal, thereby reducing arm swelling and heaviness. This effect can indirectly improve upper extremity function by reducing pain and increasing joint mobility.(Jaraczewska & Long, 2006)

Pain Management

Upper extremity pain following stroke is a significant problem that negatively affects patients' quality of life. This pain can stem from various causes, such as shoulder subluxation, spasticity, complex regional pain syndrome, or neuropathic pain.(Harrison & Field, 2015) Therapeutic taping is considered a potential tool in pain management. The pain-relieving effect of taping can be explained by several mechanisms. The most widely accepted theory is the gate control theory. According to this theory, the mechanical stimulation applied by the tape to the skin activates large-diameter afferent nerve fibers (Aβ fibers), which blocks the pain gates in the spinal cord of small-diameter pain-conducting fibers (C and Aδ fibers). This reduces pain perception by preventing pain signals from being transmitted to the brain.(Melzack, 1996) Additionally, other mechanisms of action, such as the band's ability to modulate muscle activity or spasticity, reduce edema, and stabilize subluxation, may also indirectly help reduce pain. For example, in a patient with shoulder pain following a stroke, supportive taping applied to the shoulder joint may alleviate pain by improving joint mechanics and supporting the muscles.(Jaraczewska & Long, 2006) The reduction in pain may encourage the patient to participate more actively in rehabilitation exercises, thereby accelerating functional recovery.

Subluxation Management

In post-stroke hemiplegia, shoulder subluxation is a common complication characterized by the displacement of the humeral head relative to the glenoid, either downward or anteriorly, within the glenohumeral joint. This condition arises from the weakness of the muscles stabilizing the shoulder joint (particularly the deltoid and rotator cuff muscles) due to paralysis or paresis of the upper extremity muscles. Shoulder subluxation can lead to pain, limited movement, and functional loss. Therapeutic taping can help alleviate this condition by increasing joint stability and managing shoulder subluxation. Specially designed supportive taping techniques provide additional external support to help keep the humeral head in the

glenoid cavity. When applied with specific tensions to the muscles around the shoulder (e.g., deltoid, supraspinatus) and the joint capsule, the tape can support the joint upward and reduce the downward pull caused by gravity. Additionally, the tape's provision of proprioceptive feedback may help the patient better perceive shoulder position and actively attempt to stabilize the joint using residual muscle activity. This can reduce the degree of subluxation and alleviate associated pain by promoting both passive support and active muscle engagement.(Huang et al., 2017) However, it is important to remember that taping alone is not a magical solution that can completely correct subluxation and is typically used in conjunction with other rehabilitation approaches.

RESULTS AND DISCUSSIONS

The literature examining the effect of therapeutic taping on upper extremity function in patients with ischemic stroke includes numerous studies conducted using various methods and in different patient populations. In this section, the available evidence will be summarized and grouped according to different functional areas.

Effects on Upper Extremity Motor Function

Upper extremity motor function after stroke is critical for independence in activities of daily living. Studies evaluating the effectiveness of therapeutic taping in this area have produced complex and sometimes conflicting results. For example, some randomized controlled trials (RCTs) have reported that therapeutic taping leads to a significant improvement in upper extremity motor function. In one study, therapeutic taping was shown to improve upper extremity function more than placebo taping in patients with chronic stroke.(Huang et al., 2017) Similarly, it has been noted that therapeutic taping, when combined with traditional rehabilitation, leads to significant increases in FMA-UE and Arm Function Test (AFT) scores in patients with mild to moderate stroke.(Chou et al., 2024) These studies suggest that the band may support motor learning and neuroplasticity by increasing proprioceptive feedback and providing muscle facilitation.

However, there are also studies in the literature showing that therapeutic taping has a limited effect on upper extremity motor function or does not produce a statistically significant difference. A meta-analysis emphasized that therapeutic taping has a moderate effect on upper extremity motor function after stroke, but that this effect may not always be clinically

significant.(Wang et al., 2022) Some researchers argue that taping alone may not provide significant benefits, but when combined with traditional exercise and physical therapy, it may offer more pronounced advantages. For example, one study observed an increase in manual dexterity in stroke patients who underwent therapeutic taping, but could not clearly distinguish.(Galvã et al., 2018) In general, it appears that therapeutic taping has the potential to improve upper extremity motor function, but the degree of this effect may vary depending on the patient's stroke stage, severity, the taping technique used, and the accompanying rehabilitation program. In particular, further research is needed on the direct effects of taping on activities of daily living and its role in long-term functional independence. (Tan et al., 2022)

Shoulder Subluxation and Pain Effects

Post-stroke shoulder subluxation and associated pain are significant causes of morbidity that negatively impact rehabilitation. Therapeutic taping has been studied as a promising intervention in the management of these problems. Numerous studies have indicated that therapeutic taping may be effective in reducing the degree of shoulder subluxation and alleviating post-stroke shoulder pain.(Deng et al., 2021; Huang et al., 2017; Yang et al., 2018) For example, a study demonstrated that therapeutic taping statistically significantly reduced glenohumeral subluxation and relieved shoulder pain in chronic stroke patients. The tape is thought to increase joint stability by elevating the humeral head and providing support to the rotator cuff muscles. The reduction of subluxation, coupled with reduced tension on the joint capsule and surrounding tissues, may also lead to pain relief.(Yang et al., 2018)

From a pain management perspective, several studies have reported that therapeutic taping may be superior to placebo or traditional methods in reducing post-stroke shoulder pain.(Deng et al., 2021; Yang et al., 2018) For example, A study found that taping significantly reduced shoulder pain (as measured by the Visual Analog Scale (VAS) and improved shoulder range of motion (ROM) in patients with chronic stroke. Pain reduction may accelerate functional recovery by encouraging patients to participate more willingly in rehabilitation exercises.(Gong et al., 2018) Overall, it is emphasized that therapeutic taping is a complementary treatment option for post-stroke shoulder subluxation and pain, but should not be considered a sole solution.

Effects on Spasticity

Post-stroke spasticity is a significant problem characterized by excessive muscle tone and involuntary contractions, leading to limited movement, pain, and loss of functional independence. The effects of therapeutic taping on spasticity have been discussed in the literature with

varying results.(In et al., 2021; Karadag-Saygi et al., 2010) Some studies suggest that taping can be effective in reducing spasticity(In et al., 2021), particularly when applied with muscle relaxant or inhibitory techniques. For example, one study reported that therapeutic taping applied to upper extremity flexor muscles in stroke patients resulted in significant reduction.(Karadag-Saygi et al., 2010) This effect has been attributed to the tape's ability to reduce muscle tone by reducing tension on muscle fibers and modulating muscle spindle activity. The tape's ability to lift the skin surface and create a relaxing effect on the fascia may also contribute to reducing spasticity. (Cai et al., 2016)

Different Application Protocols and Comparison of Effects

Therapeutic taping can be used with various application protocols, depending on the practitioner's knowledge and the patient's needs. These different techniques are differentiated by parameters such as the amount of tape tension, the cut shape, the direction of application, and the duration of application, and target different mechanisms of action. The most commonly used techniques in stroke rehabilitation include muscle support (facilitation/inhibition), ligament support, and lymphatic drainage techniques.(Hewetson et al., 2009) The effects of each of these techniques on upper extremity function may vary, and these differences have been compared by researchers.

Muscle support techniques are generally used to increase the activation of weak or paretic muscles (facilitation) or to reduce the tone of spastic muscles (inhibition). In facilitation techniques, the tape is applied with 15-35% tension from the beginning of the muscle to the end, while in inhibition techniques, the tape is applied with a lower tension (0-15%) from the end of the muscle to the beginning. Research has shown that facilitative taping can improve shoulder elevation and elbow flexion by increasing the activity of proximal upper extremity muscles (deltoid, biceps). Conversely, inhibitory taping can increase range of motion and facilitate hygiene by decreasing the tone of the elbow and wrist flexor muscles in patients with flexor spasticity. The effects of these different applications on motor function and spasticity have generally been evaluated by targeting specific muscle groups.(Constantinou & Brown, 2010; Fukui et al., 2017)

Ligament support techniques are used specifically in cases of joint instability, such as shoulder subluxation. In these techniques, the tape is applied with higher tension (50-75%) and generally at specific anatomical points around the joint, mimicking the stabilizing effect of the ligaments or muscles surrounding the joint. This taping helps maintain the humeral head within the glenoid cavity, increasing the mechanical stability of the shoulder.(Hewetson et al., 2009) This is a critical approach to maintaining joint integrity, particularly during weight-bearing and active movement.

Thirdly, lymphatic drainage techniques focus on reducing upper extremity edema after stroke. In these techniques, the tape is applied, usually with very low or no tension, from the edema to the lymph nodes by cutting it into a "fan" or "octopus" shape on the skin. This creates a space between the skin and subcutaneous tissues, facilitating the movement of lymph fluid and mobilizing edema.(Hewetson et al., 2009) Research has shown that these techniques are effective in reducing hand and arm edema, indirectly contributing to functional recovery by relieving pain and increasing range of motion. For example, one study demonstrated significant improvements in hand edema and wrist range of motion in stroke patients who underwent lymphatic taping.(Jaraczewska & Long, 2006) These techniques are particularly preferred in cases where edema causes pain and limited movement.

While the number of studies directly comparing the effects of these different taping techniques is limited, the literature indicates that each technique is designed to address a specific clinical problem and produces different results. For example, an inhibitory technique is used to reduce spasticity, while a facilitative technique is preferred to alleviate muscle weakness. While techniques that provide mechanical support are preferred for shoulder subluxation, lymphatic techniques are more suitable for edema. Therefore, the effectiveness of therapeutic taping depends on the application of the correct technique for the correct indication and according to individual patient needs. Clinicians should carefully evaluate the patient's specific motor, sensory, and orthopedic issues to select the most appropriate taping protocol. The potential benefits of combining or sequential applications of different techniques also constitute an interesting area for future research.

CONCLUSION

Upper extremity dysfunction after ischemic stroke is a common morbidity that significantly impacts patients' quality of life and independence. This review summarizes the current literature examining the potential role and mechanisms of action of therapeutic taping (kinesiology taping) in managing these functional losses. The findings suggest that therapeutic taping may contribute to upper extremity functional recovery by enhancing proprioceptive feedback, modulating muscle activity, reducing edema, managing pain, and stabilizing shoulder subluxation. There is consistent evidence that therapeutic taping is beneficial, particularly in reducing shoulder subluxation and post-stroke shoulder pain. More mixed and sometimes conflicting results have been obtained regarding its effects on

spasticity and direct motor function, highlighting the importance of taping technique, application duration, and individual patient characteristics.

Different application protocols have been found to have varying effects depending on the targeted clinical problem. Muscle-supporting techniques facilitate weak muscles, while inhibitory techniques have the potential to reduce spasticity. Ligament-supporting techniques increase joint stability, and lymphatic techniques are effective in resolving edema. This highlights the need for a personalized, evidence-based approach to integrating therapeutic taping into stroke rehabilitation.

In conclusion, therapeutic taping can be incorporated as a complementary intervention into rehabilitation programs aimed at improving upper extremity functional status in patients with ischemic stroke. However, it is important to remember that taping is not a stand-alone solution and should always be used as part of a comprehensive rehabilitation program. Future research should more clearly demonstrate the clinical benefits of therapeutic taping through standardized application protocols, long-term effects, and effectiveness across stroke stages and severities.

REFERENCES

Anvar, C. (2024). Lymphascial kinesiology taping for peripheral arterial disease and chronic venous insufficiency. Wounds, 20(2), 26.

Bell, A., & Muller, M. (2013). Effects of kinesio tape to reduce hand edema in acute stroke. Topics in stroke rehabilitation, 20(3), 283-288.

Bustamante, A., Garcia-Berrocoso, T., Rodriguez, N., Llombart, V., Ribo, M., Molina, C., & Montaner, J. (2016). Ischemic stroke outcome: A review of the influence of post-stroke complications within the different scenarios of stroke care. European journal of internal medicine, 29, 9-21.

Cai, C., Au, I., An, W., & Cheung, R. (2016). Facilitatory and inhibitory effects of Kinesio tape: Fact or fad? Journal of science and medicine in sport, 19(2), 109-112.

Castaño, P. R. L., Laiseca, Y. A. R., Suárez, D. P. M., Papamija, D. B. C., & Urriago, G. E. L. (2020). Effects of kinesiotaping combined with the motor relearning method on upper limb motor function in adults with hemiparesis after stroke. Journal of Bodywork and Movement Therapies, 24(4), 546-553.

Chou, C.-H., Lee, Y.-Y., Chen, P.-C., Leong, C.-P., & Huang, Y.-C. (2024). Effects of Kinesiotaping on upper limb function and daily activities in subacute or chronic stroke survivors: A randomized control study. NeuroRehabilitation, 54(4), 629-637.

Constantinou, M., & Brown, M. (2010). Therapeutic taping for musculoskeletal conditions-E-Book. Elsevier Health Sciences.

Deng, P., Zhao, Z., Zhang, S., Xiao, T., & Li, Y. (2021). Effect of kinesio taping on hemiplegic shoulder pain: a systematic review and meta-analysis of randomized controlled trials. Clinical Rehabilitation, 35(3), 317-331.

Feigin, V. L., Brainin, M., Norrving, B., Martins, S. O., Pandian, J., Lindsay, P., F Grupper, M., & Rautalin, I. (2025). World stroke organization: global stroke fact sheet 2025. International Journal of Stroke, 20(2), 132-144.

Fukui, T., Otake, Y., & Kondo, T. (2017). The effects of new taping methods designed to increase muscle strength. Journal of Physical Therapy Science, 29(1), 70-74.

Galvã, J., Silva, M. d. D. C., Tenó, J., dos Anjos, C. C., & Soutinho, R. S. R. (2018). Effect of kinesio taping on hand function in hemiparetic patients. World Journal of Neuroscience, 8(2), 293-302.

Gong, W., Wang, L.-H., Guo, B.-Z., Du, J.-N., Yu, J., & Chen, H.-X. (2018). Effect of kinesio taping on shoulder pain after stroke. Journal of Hanainan Medical University [online], 24(20), 77-80.

Harrison, R. A., & Field, T. S. (2015). Post stroke pain: identification, assessment, and therapy. Cerebrovascular diseases, 39(3-4), 190-201.

Hewetson, T. J., Austin, K., Gwynn-Brett, K., & Marshall, S. (2009). An illustrated guide to taping techniques: Principles and practice. Elsevier Health Sciences.

Huang, Y.-C., Chang, K.-H., Liou, T.-H., Cheng, C.-W., Lin, L.-F., & Huang, S.-W. (2017). Effects of Kinesio taping for stroke patients with hemiplegic shoulder pain: a double-blind, randomized, placebo-controlled study. Journal of rehabilitation medicine, 49(3), 208-215.

In, T.-s., Jung, J.-h., Jung, K.-s., & Cho, H.-y. (2021). Effect of sit-to-stand training combined with taping on spasticity, strength, gait speed and quality of life in patients with stroke: A randomized controlled trial. Life, 11(6), 511.

Jaraczewska, E., & Long, C. (2006). Kinesio® taping in stroke: improving functional use of the upper extremity in hemiplegia. Topics in stroke rehabilitation, 13(3), 31-42.

Karadag-Saygi, E., Cubukcu-Aydoseli, K., Kablan, N., & Ofluoglu, D. (2010). The role of kinesiotaping combined with botulinum toxin to reduce plantar flexors spasticity after stroke. Topics in stroke rehabilitation, 17(4), 318-322.

Melzack, R. (1996). Gate control theory: On the evolution of pain concepts. Pain forum,

Mostafavifar, M., Wertz, J., & Borchers, J. (2012). A systematic review of the effectiveness of kinesio taping for musculoskeletal injury. The Physician and sportsmedicine, 40(4), 33-40.

Shiber, J. R., Fontane, E., & Adewale, A. (2010). Stroke registry: hemorrhagic vs ischemic strokes. The American journal of emergency medicine, 28(3), 331-333.

Tan, B., Jia, G., Song, Y., & Jiang, W. (2022). Effect of kinesiotaping on pain relief and upper limb function in stroke survivors: A systematic review and meta-analysis. American Journal of Translational Research, 14(5), 3372.

Tuthill, J. C., & Azim, E. (2018). Proprioception. Current Biology, 28(5), R194-R203.

Wang, Y., Li, X., Sun, C., & Xu, R. (2022). Effectiveness of kinesiology taping on the functions of upper limbs in patients with stroke: a meta-analysis of randomized trial. Neurological Sciences, 43(7), 4145-4156.

Yang, L., Yang, J., & He, C. (2018). The effect of kinesiology taping on the hemiplegic shoulder pain: a randomized controlled trial. Journal of healthcare engineering, 2018(1), 8346432.

Yim, J., & Kim, B. (2024). Effectiveness of shoulder taping in treating hemiplegic shoulder Subluxation: a randomized controlled study of 35 patients. Medical Science Monitor: International Medical Journal of Experimental and Clinical Research, 30, e944222-944221.

Dystonia: A Comprehensive Review of Its Etiology, Pathophysiology, and Modern Therapeutic Approaches

Mehmet SÖNMEZ[1]

1- Asst. Prof. Dr., Mehmet SÖNMEZ, Department of Orthopedical Rehabilitation, Erzurum Technical University Health Science Faculty, Physiotherapy and Rehabilitation, mehmet.sonmez@erzurum.edu.tr, ORCID: 0000-0002-3617-9087 Tel:444-5-388-(2739)

ABSTRACT

Purpose: This review aims to provide a comprehensive overview of the clinical, etiological, and pathophysiological aspects of dystonia, while also summarizing contemporary treatment methods. The section aims to serve as a reference source for both healthcare professionals and readers interested in the subject.

Approach Used: The approach synthesizes existing scientific literature to explain the disorder's heterogeneity, classifying it by affected body region, age of onset, and etiology (primary and secondary). It examines the underlying mechanisms and therapeutic strategies based on an in-depth analysis of current research.

Key Results: The pathophysiology of dystonia involves a complex interplay of basal ganglia, cerebellar, and cortical dysfunction, including impaired sensorimotor integration and abnormal plasticity. While the prevalence of dystonia varies, it is not considered a life-shortening condition, but significantly impacts a patient's quality of life.

Important Conclusions: An accurate diagnosis and a personalized, multidisciplinary treatment plan—incorporating pharmacological options like botulinum toxin injections, surgical interventions such as Deep Brain Stimulation (DBS), and supportive therapies—are crucial for effective management. This underscores the importance of a holistic approach to address the motor and psychosocial challenges of the disease.

Keywords: Dystonia, Pathophysiology, Basal Ganglia, Botulinum Toxin, Deep Brain Stimulation, Sensorimotor Integration

INTRODUCTION

Dystonia is a complex neurological condition characterized by involuntary, continuous, or intermittent muscle contractions resulting from a disorder in the brain's movement control system. These contractions cause repetitive twisting movements, abnormal postures, or tremors in the patient's body. Compared to more commonly known movement disorders such as Parkinson's disease or essential tremor, dystonia is less recognized, which can often lead to misdiagnosis or delayed diagnosis.(Balint et al., 2018) However, this condition is a significant health issue that seriously affects individuals' quality of life, social interactions, and occupational abilities,

requiring accurate and timely diagnosis and comprehensive treatment approaches. Therefore, addressing all aspects of dystonia—from its etiology to its pathophysiology, different types, and modern treatment methods—is of great importance for both healthcare professionals and patients and their families.

This section aims to bring together scientific information on dystonia, providing an in-depth explanation of the disease's clinical and etiological characteristics, underlying pathophysiological mechanisms, prevalence, and different types. By combining existing data with the most up-to-date treatment approaches and future research areas, a comprehensive and enlightening perspective on the complex world of dystonia will be presented.

This section aims to provide a detailed explanation of the clinical and etiological characteristics of dystonia, its pathophysiological mechanisms, prevalence, types, and current treatment approaches. By providing information on a wide range of topics, from the symptoms of dystonia to genetic and environmental factors, diagnostic methods, and pharmacological and surgical treatments, it will emphasize the multidisciplinary nature of the disease. The section aims to serve as a reference source for both healthcare professionals and readers interested in the subject.

GENERAL CHARACTERISTICS

1. Definition of Dystonia

Dystonia is a syndrome characterized by involuntary, sustained muscle contractions that result in twisting and repetitive movements or abnormal postures. These contractions arise from the simultaneous contraction of agonist and antagonist muscles (co-contraction). In addition to involuntary muscle contractions, dystonia may exhibit a “task-specific” feature; that is, it is triggered while attempting to perform a specific action (e.g., handwriting dystonia). Patients often use a sensory trick to alleviate the abnormal postures or movements caused by the contractions (e.g., touching the chin may alleviate cervical dystonia).(Albanese et al., 2019)

2. Etiology

Dystonia is a complex and heterogeneous disorder, making it difficult to attribute it to a single cause. Generally, the etiology of dystonia is divided into two main categories: primary (idiopathic) dystonia and secondary dystonia. This classification is critical for understanding the underlying causative factors and reaching a correct diagnosis.(Kojovic et al., 2013)

Primary (Idiopathic) Dystonia

This category encompasses cases where dystonia is the only main clinical symptom and there is no evidence of another neurological disease or brain injury. Genetic factors underlie primary dystonia. These forms, also called genetic dystonias (Dystonia plus, Hereditary dystonias), are often associated with specific gene mutations. One of the most well-known genes is the DYT1 (TOR1A) gene. A mutation in this gene is the most common cause of

generalized dystonia, especially early-onset dystonia. Approximately 30-40% of individuals with DYT1 mutations develop dystonia symptoms, while the remainder may be asymptomatic (incomplete penetrance). This suggests that environmental or epigenetic factors, as well as genetic predisposition, may play a role.(Grütz & Klein, 2021)

In addition to DYT1, many other genes, including DYT6 (THAP1), DYT5 (GCH1), and DYT11 (SGCE), are known to cause dystonia. DYT5 gene mutations lead to dopamine-responsive dystonia (DRD) and often respond dramatically to L-dopa treatment. This genetic heterogeneity complicates understanding the causes of dystonia and developing personalized treatment approaches.(Grütz & Klein, 2021)

Secondary Dystonia

Secondary dystonia is a type of dystonia that occurs as a result of another underlying neurological condition or an environmental factor. In these cases, a structural or chemical damage in the brain causes dystonia symptoms.(Schneider & Bhatia, 2010) The most common causes are:

• Medication Use: Long-term use of antipsychotic medications, in particular, can cause a persistent form of dystonia called tardive dystonia. Anti-nausea medications such as metoclopramide can also cause this condition.(Schneider & Bhatia, 2010)

• Brain Injury: Damage to the basal ganglia or thalamus due to stroke, traumatic brain injury (TBI), tumors, infections (e.g., encephalitis), or oxygen deprivation can lead to secondary dystonia.(Schneider & Bhatia, 2010)

• Neurodegenerative and Metabolic Diseases: Wilson's disease, various lysosomal storage diseases, mitochondrial diseases, and rare metabolic disorders such as methylmalonic acidemia are examples of conditions where dystonia is present in the clinical picture.(Schneider & Bhatia, 2010)

• Other Neurological Diseases: Some neurological diseases, such as Parkinson's disease, Huntington's disease, and multiple sclerosis (MS), can also present with dystonia-like symptoms or cause dystonia.(Schneider & Bhatia, 2010)

This etiological classification plays a key role in both making a correct diagnosis and determining the treatment strategy. For example, while symptomatic treatment is usually the goal in primary dystonia, treatment of the underlying cause may become the priority in secondary dystonia.(Tierney & Lozano, 2012)

3. Pathophysiology

The pathophysiology of dystonia is based on functional disorders in the complex neural networks responsible for movement control in the brain. In particular, abnormalities in the interactions between the basal ganglia, cerebellum, and motor cortex play a key role in the onset of dystonia.(Brüggemann, 2021) Although the exact mechanism is still under

investigation, current scientific evidence converges around several fundamental hypotheses.

Basal Ganglia Dysfunction

The basal ganglia are deep brain structures responsible for initiating, regulating, and inhibiting motor movements. Normally, the basal ganglia suppress unwanted movements while ensuring that targeted movements occur smoothly. In dystonia, this balance is disrupted. According to hypotheses, there is a deviation in the balance between the direct and indirect pathways of the basal ganglia. It is thought that the direct pathway is overactive, while the indirect pathway is underactive. This imbalance leads to faulty signals being sent to the motor cortex, resulting in involuntary muscle contractions. In particular, it is thought that there is a decrease in the function of GABA (gamma-aminobutyric acid) neurons in the basal ganglia. GABA is the brain's primary inhibitory neurotransmitter, and a decrease in this inhibitory effect weakens the basal ganglia's control over the motor cortex, leading to excessive and uncontrolled muscle activity. (Brüggemann, 2021; Hallett, 2008)

Cerebellar Abnormalities

While traditionally considered a basal ganglia disease, recent research suggests that the cerebellum also plays a significant role in the pathophysiology of dystonia. The cerebellum is responsible for the coordination, timing, and motor learning of movement. Abnormalities in the connections between the cerebellum and basal ganglia have been identified in patients with dystonia. Dysfunction in the cerebellum can contribute to the mistiming of motor signals and impaired coordination between muscles. This may explain the abnormal muscle contraction during repetition of a movement, particularly in task-specific dystonias.(Avanzino & Abbruzzese, 2012; Brüggemann, 2021)

Impairment of Sensorimotor Integration

One of the most distinctive features of dystonia is impaired sensorimotor integration. The brain integrates both motor commands and sensory feedback (muscle position, joint tension, etc.) when planning and executing movement. In patients with dystonia, errors in processing this sensory information and integrating it into the motor system are thought to occur. For example, in writer's cramp, a focal dystonia, abnormal processing of sensory signals from the fingers and hand during the act of writing leads to involuntary and abnormal muscle contractions. This helps explain the task-specific nature of the disorder.(Avanzino et al., 2015; Desrochers et al., 2019)

Cortical Plasticity and Disinhibition

The motor cortex of the brain plays a central role in the pathophysiology of dystonia. In patients with dystonia, abnormal plasticity of the motor cortex

has been observed, meaning the motor map is abnormally reorganized. Normally, the brain expands the cortical areas representing the muscle groups required to perform a task. In dystonia, this plasticity is abnormal, and the separation (segregation) between adjacent muscle groups is disrupted. This causes the attempt to move a muscle to also contract neighboring muscles not normally involved in the movement (co-contraction).(Quartarone & Pisani, 2011)

Furthermore, cortical disinhibition in the motor cortex has been suggested as an important mechanism. Transcranial Magnetic Stimulation (TMS) studies have shown increased motor cortex excitability and decreased cortical inhibition in patients with dystonia. This decreased inhibition leads to excessive and uncontrolled propagation of motor signals, paving the way for involuntary muscle contractions.(Lozeron et al., 2016; Quartarone, 2013)

In summary, the pathophysiology of dystonia is not a single mechanism, but rather the result of complex and disrupted interactions between the basal ganglia, cerebellum, and motor cortex. These disruptions manifest through processes such as improper processing of sensory information, motor disinhibition, and abnormal cortical plasticity, leading to involuntary movements and abnormal postures that impact the patient's life. This multifaceted pathophysiological understanding is a vital step in the development of new, targeted treatment strategies for dystonia.

4. Prevalence and Mortality Rate

Although dystonia is less common in the general population than other movement disorders, its prevalence varies significantly across geographic regions, ethnicities, and research methods. The prevalence of the disease—the number of people affected by dystonia at any given time—is difficult to precisely determine. This is primarily due to the existence of different types of dystonia, the variability in symptom severity, and the fact that some cases go undiagnosed.(Steeves et al., 2012) Large-scale epidemiological studies estimate the prevalence of dystonia in the general population to be between 10 and 50 per 100,000 people.(Defazio et al., 2004)

These prevalence figures vary significantly depending on the type of dystonia. For example, focal dystonias are much more common than generalized dystonias. Cervical dystonia (neck dystonia) and blepharospasm (eyelid dystonia) are among the most common types of focal dystonia. The prevalence of these focal forms can be as high as 100 per 100,000 in some studies. On the other hand, early-onset generalized dystonias, and particularly genetic forms (e.g., DYT1 dystonia), are rarer and generally have lower prevalence.(Dressler et al., 2022; Muller et al., 2002)

Age also has a significant impact on prevalence. Dystonias that begin in childhood and adolescence are generally due to genetic causes and tend to generalize. Dystonias that begin in adulthood are more likely to remain focal and are generally considered idiopathic (of unknown cause). However,

recent studies have suggested that genetic factors or small brain lesions underlie some cases of focal dystonia in adults.(O'riordan et al., 2004)
Regarding mortality, dystonia alone is not considered a life-shortening condition. The disease is generally non-progressive and does not pose a life-threatening condition. However, in some patients with severe dystonia, particularly generalized dystonia, secondary complications related to the disease may arise.(Bailey et al., 2022) For example, difficulty swallowing (dysphagia) can lead to aspiration pneumonia, or respiratory failure can develop in cases where the respiratory muscles are affected. Such secondary complications can indirectly impact a patient's life expectancy. Most significant is the impact of dystonia on quality of life. Involuntary contractions and abnormal postures restrict daily activities (walking, eating, talking), causing social isolation and occupational difficulties. Accompanying symptoms such as pain, sleep disturbances, and depression significantly negatively impact patients' overall health and well-being. Therefore, managing dystonia requires a comprehensive approach that not only treats motor symptoms but also improves patients' quality of life.(Bailey et al., 2022)

5. Classification of Dystonia

Dystonia is a complex disorder, therefore, it is classified in various ways based on its clinical features, age of onset, and etiology. This classification is a critical guide in making an accurate diagnosis, predicting its course, and determining the most appropriate treatment strategy.

Classification by Affected Body Region

This classification focuses on the part of the body affected by dystonia and is the most frequently used method in clinical practice.

• Focal Dystonia: Affects a single body region and is the most common type of dystonia.

o Cervical Dystonia (Spasmodic Torticollis): Affects the neck muscles, causing the head to bend, rotate, or tilt forward or backward abnormally. It is usually painful and significantly reduces the patient's quality of life.

o Blepharospasm: Characterized by involuntary contraction of the eyelid muscles. It can cause the eyes to squint or close completely, negatively impacting vision. It usually affects both eyes. o Laryngeal Dystonia (Spasmodic Dysphonia): Affects the vocal cords. It causes the voice to sound shaky, choppy, or muffled during speech.

o Writer's Cramp: Causes involuntary contractions in the hand and arm muscles during activities requiring fine motor skills (e.g., writing, playing a musical instrument). This condition is also known as task-specific dystonia. (di Biase et al., 2022)

• Segmental Dystonia: Affects two or more adjacent areas of the body. For example, simultaneous impaction of the arm and neck muscles.

• Multifocal Dystonia: Affects two or more non-adjacent areas of the body. For example, simultaneous dystonia in one arm and one leg.

• Generalized Dystonia: Affects a large part of the body, including the trunk, arms, and legs. It usually begins at an early age and is genetically determined. This type of dystonia is the most severe and restricts activities of daily living.
• Hemidystonia: Affects only one side of the body (right or left). It usually occurs as a result of a lesion (stroke, tumor, etc.) located on the opposite side of the brain.(di Biase et al., 2022)

Classification by Age of Onset

This classification helps understand the course of the disease and its possible etiology based on the age of onset.
• Early-Onset Dystonia: Usually begins in childhood or adolescence (before age 20). These dystonias are usually genetic in origin and tend to begin focally and become generalized over time.
• Late-Onset Dystonia: Usually begins in adulthood (after age 20). These dystonias tend to remain focal and are less likely to become generalized.(Albanese et al., 2025)

Classification by Etiology

This classification is based on the underlying cause of the dystonia and directly impacts the treatment strategy.
• Primary (Idiopathic) Dystonia: This type of dystonia is not associated with any known brain damage or disease. Genetic factors are usually involved.
• Secondary Dystonia: Dystonia that occurs due to brain injury, drug use, or another neurological disease.(Albanese et al., 2025)
• Hereditary Dystonia: These are genetically transmitted and inherited forms of dystonia. The most common is the DYT1 gene mutation, which causes early-onset generalized dystonia.(Albanese et al., 2025)

6. Treatment Methods

Dystonia treatment is a multifaceted approach that aims to relieve symptoms, improve functionality, and improve the patient's quality of life. The treatment plan is personalized based on the patient's dystonia type, symptom severity, age of onset, and underlying cause. Treatment is typically conducted by a multidisciplinary team that combines pharmacological, surgical, and rehabilitation approaches.(Jankovic, 2006)

Pharmacological Treatments

• Botulinum Toxin (Botox) Injections: This is considered the gold standard for the treatment of focal dystonias. Botulinum toxin prevents muscle contraction by blocking the release of acetylcholine at the neuromuscular junction. It is injected directly into the patient's contracting muscles by a neurologist. The effects of the injection begin within a few days and usually last for 3-4 months. Therefore, regular injections are necessary to keep symptoms under control. This method has a high success rate, especially in focal forms such as cervical dystonia, blepharospasm, and laryngeal dystonia.(Balash & Giladi, 2004)

Oral Medications

Various oral medications attempt to control dystonia symptoms by regulating the neurotransmitter balance in the brain.

o Anticholinergics: Drugs such as trihexyphenidyl and benztropine relieve spasms by reducing acetylcholine activity. They can be particularly effective in generalized dystonia, which begins in childhood. However, they should be used with caution due to side effects such as dry mouth, blurred vision, and memory problems.(Jankovic, 2013)

o Benzodiazepines: Drugs such as diazepam and clonazepam provide muscle relaxation by acting as inhibitors on GABA receptors.(Jankovic, 2013)

o Baclofen: This GABA B receptor agonist can be particularly useful in spinal dystonia and lower extremity dystonia. In severe cases, an intrathecal baclofen pump can provide more effective results by delivering medication directly into the spinal fluid.(Jankovic, 2006)

o Dopaminergic Agents: In dopamine-responsive dystonias (DRD), levodopa-containing medications can provide dramatic relief. This demonstrates the vital importance of accurate diagnosis. (Jankovic, 2006)

Surgical Treatments

Surgical options are considered in cases of severe dystonia that do not respond to medication and significantly impact quality of life.

• Deep Brain Stimulation (DBS): This is the most effective surgical treatment for primary generalized or segmental dystonia. Electrodes are placed in specific areas of the basal ganglia in the brain (specifically the globus pallidus internus (GPi)). These electrodes regulate abnormal brain activity by delivering a continuous electrical current through a pacemaker (neurostimulator) placed under the skin of the chest. The effectiveness of DBS increases over time and provides significant symptom relief in patients.(Cury et al., 2018)

• Selective Peripheral Denervation: This surgical technique is used primarily in cases of cervical dystonia. A portion of the nerve branches supplying the muscles in the neck are surgically severed to prevent contraction. This method causes permanent muscle weakening and can be effective in properly selected patients.(Bergenheim et al., 2015)

Rehabilitation and Supportive Treatments

• Physical and Occupational Therapy: These therapies are vital for increasing muscle flexibility, improving posture, and facilitating activities of daily living. Physiotherapists help reduce muscle spasms with specialized exercises and stretching techniques.(Dressler & Adib Saberi, 2016)

• Speech Therapy: Therapies aimed at improving voice control are used in conditions that cause speech difficulties, such as laryngeal dystonia.(Dressler et al., 2016)

• Psychological Support: Dystonia can profoundly impact patients' psychosocial lives. Depression, anxiety, and social isolation are common problems. Psychological counseling or therapy helps patients cope with these challenges.(O'Connor et al., 2023)

CONCLUSION

Dystonia is a complex neurological movement disorder characterized by involuntary muscle contractions and abnormal postures, which significantly impacts quality of life. Throughout this chapter, we have examined the multifaceted nature of dystonia in detail, from its etiology (primary and secondary causes) to its pathophysiological mechanisms (basal ganglia, cerebellum, and motor cortex dysfunction). We have seen the broad clinical spectrum of the disease, ranging from focal to generalized forms. Furthermore, it was emphasized that the prevalence of dystonia varies according to geographic and genetic factors, but that it is not a condition that shortens lifespan on its own; its primary impact is on patient functionality and quality of life.

It was emphasized that treatment approaches should be comprehensive and personalized, including botulinum toxin injections, oral medications, and modern surgical techniques such as deep brain stimulation. Finally, we have demonstrated the importance of physical and psychological support in improving the overall well-being of individuals living with dystonia. The understanding and management of dystonia is an ever-evolving field requiring a multidisciplinary approach, and this chapter aims to be an essential resource for patients struggling with this challenging condition and the professionals who support them.

REFERENCES

Albanese, A., Bhatia, K. P., Fung, V. S., Hallett, M., Jankovic, J., Klein, C., Krauss, J. K., Lang, A. E., Mink, J. W., & Pandey, S. (2025). Definition and Classification of Dystonia. Movement disorders.

Albanese, A., Di Giovanni, M., & Lalli, S. (2019). Dystonia: diagnosis and management. European journal of neurology, 26(1), 5-17.

Avanzino, L., & Abbruzzese, G. (2012). How does the cerebellum contribute to the pathophysiology of dystonia? Basal Ganglia, 2(4), 231-235.

Avanzino, L., Tinazzi, M., Ionta, S., & Fiorio, M. (2015). Sensory-motor integration in focal dystonia. Neuropsychologia, 79, 288-300.

Bailey, G. A., Rawlings, A., Torabi, F., Pickrell, O., & Peall, K. J. (2022). Adult-onset idiopathic dystonia: A national data-linkage study to determine epidemiological, social deprivation, and mortality characteristics. European journal of neurology, 29(1), 91-104.

Balash, Y., & Giladi, N. (2004). Efficacy of pharmacological treatment of dystonia: evidence-based review including meta-analysis of the effect of botulinum toxin and other cure options. European journal of neurology, 11(6), 361-370.

Balint, B., Mencacci, N. E., Valente, E. M., Pisani, A., Rothwell, J., Jankovic, J., Vidailhet, M., & Bhatia, K. P. (2018). Dystonia. Nature reviews Disease primers, 4(1), 25.

Bergenheim, A. T., Nordh, E., Larsson, E., & Hariz, M. I. (2015). Selective peripheral denervation for cervical dystonia: long-term follow-up. Journal of Neurology, Neurosurgery & Psychiatry, 86(12), 1307-1313.

Brüggemann, N. (2021). Contemporary functional neuroanatomy and pathophysiology of dystonia. Journal of Neural Transmission, 128(4), 499-508.

Cury, R. G., Kalia, S. K., Shah, B. B., Jimenez-Shahed, J., Prashanth, L. K., & Moro, E. (2018). Surgical treatment of dystonia. Expert review of neurotherapeutics, 18(6), 477-492.

Defazio, G., Abbruzzese, G., Livrea, P., & Berardelli, A. (2004). Epidemiology of primary dystonia. The Lancet Neurology, 3(11), 673-678.

Desrochers, P., Brunfeldt, A., Sidiropoulos, C., & Kagerer, F. (2019). Sensorimotor control in dystonia. Brain sciences, 9(4), 79.

di Biase, L., Di Santo, A., Caminiti, M. L., Pecoraro, P. M., & Di Lazzaro, V. (2022). Classification of dystonia. Life, 12(2), 206.

Dressler, D., & Adib Saberi, F. (2016). Rehabilitation of dystonia. In Movement disorders rehabilitation (pp. 67-81). Springer.

Dressler, D., Altenmueller, E., Bhidayasiri, R., Bohlega, S., Chana, P., Chung, T. M., Frucht, S., Garcia-Ruiz, P. J., Kaelin, A., & Kaji, R. (2016). Strategies for treatment of dystonia. Journal of Neural Transmission, 123(3), 251-258.

Dressler, D., Altenmüller, E., Giess, R., Krauss, J. K., & Adib Saberi, F. (2022). The epidemiology of dystonia: the Hannover epidemiology study. Journal of neurology, 269(12), 6483-6493.

Grütz, K., & Klein, C. (2021). Dystonia updates: definition, nomenclature, clinical classification, and etiology. Journal of Neural Transmission, 128(4), 395-404.

Hallett, M. (2008). Pathophysiology of dystonia. Therapeutics of Parkinson's Disease and Other Movement Disorders, 203-215.

Jankovic, J. (2006). Treatment of dystonia. The Lancet Neurology, 5(10), 864-872.

Jankovic, J. (2013). Medical treatment of dystonia. Movement disorders, 28(7), 1001-1012.

Kojovic, M., Pareés, I., Kassavetis, P., Palomar, F. J., Mir, P., Teo, J. T., Cordivari, C., Rothwell, J. C., Bhatia, K. P., & Edwards, M. J. (2013). Secondary and primary dystonia: pathophysiological differences. Brain, 136(7), 2038-2049.

Lozeron, P., Poujois, A., Richard, A., Masmoudi, S., Meppiel, E., Woimant, F., & Kubis, N. (2016). Contribution of TMS and rTMS in the understanding of the pathophysiology and in the treatment of dystonia. Frontiers in neural circuits, 10, 90.

Muller, J., Kiechl, S., Wenning, G., Seppi, K., Willeit, J., Gasperi, A., Wissel, J., Gasser, T., & Poewe, W. (2002). The prevalence of primary dystonia in the general community. Neurology, 59(6), 941-943.

O'Connor, S., Hevey, D., & O'Keeffe, F. (2023). Illness perceptions, coping, health-related quality of life and psychological outcomes in cervical dystonia. Journal of Clinical Psychology in Medical Settings, 30(1), 129-142.

O'riordan, S., Raymond, D., Lynch, T., Saunders-Pullman, R., Bressman, S., Daly, L., & Hutchinson, M. (2004). Age at onset as a factor in determining the phenotype of primary torsion dystonia. Neurology, 63(8), 1423-1426.

Quartarone, A. (2013). Transcranial magnetic stimulation in dystonia. Handbook of clinical neurology, 116, 543-553.
Quartarone, A., & Pisani, A. (2011). Abnormal plasticity in dystonia: disruption of synaptic homeostasis. Neurobiology of disease, 42(2), 162-170.
Schneider, S., & Bhatia, K. (2010). Secondary dystonia–clinical clues and syndromic associations. European journal of neurology, 17, 52-57.
Steeves, T. D., Day, L., Dykeman, J., Jette, N., & Pringsheim, T. (2012). The prevalence of primary dystonia: a systematic review and meta-analysis. Movement disorders, 27(14), 1789-1796.
Tierney, T. S., & Lozano, A. M. (2012). Surgical treatment for secondary dystonia. Movement disorders, 27(13), 1598-1605.