



LITERATURE REVIEW ON NEUROLOGICAL EXAMINATION

Sreenu Thalla^{1*}, Dandila Rupa¹, Jonnalagadda Vikhil¹, Aluri.kusumanjali¹, Anthony Raju Yanamadri¹, Muli Sagar Anil Kumar Reddy¹ and Puttagunta Srinivasa Babu²

¹Department of Pharmacology, Vignan Pharmacy College (Autonomous), Vadlamudi, Guntur, Andhra Pradesh, India.

²Department of Pharmaceutics, Vignan Pharmacy College (Autonomous), Vadlamudi, Guntur, Andhra Pradesh, India.



*Corresponding Author: Dr. Sreenu Thalla

Department of Pharmacology, Vignan Pharmacy College (Autonomous), Vadlamudi, Guntur, Andhra Pradesh, India.

Article Received on 16/10/2024

Article Revised on 06/11/2024

Article Accepted on 26/11/2024

ABSTRACT

This literature review explores the evolving methodologies and clinical significance of neurological examinations in diagnosing and managing disorders of the central and peripheral nervous systems. Neurological examinations are cornerstone procedures in clinical neurology, providing essential insights into motor, sensory, cognitive, and autonomic functions. This review synthesizes current research and historical advancements in the field, focusing on the reliability, validity, and limitations of traditional examination techniques, such as reflex testing, cranial nerve assessment, and coordination evaluation. Additionally, it examines the integration of modern technologies, including neuroimaging and digital tools, which complement and enhance traditional assessments. The review highlights emerging trends, such as the use of artificial intelligence and machine learning, in analyzing examination data, offering promising avenues for early diagnosis and personalized treatment strategies. By evaluating key studies, this review underscores the importance of a holistic approach that combines clinical acumen with technological innovation in advancing neurological care.

KEYWORDS: Motor function, Sensory assessment, Cranial nerve evaluation, Reflex testing, Coordination assessment, Neuroimaging.

INTRODUCTION

A neurological assessment is used to assess the sensory neuron and motor responses, especially reflexes, to determine whether the nervous system is impaired. This typically includes a physical examination and a review of the patient's medical history, but not deeper investigation such as neuroimaging. The neurological assessment helps to identify discrete abnormalities with possible precise location of the problem relevant to neurological system.

A complete neurological assessment can be done by using the following steps. Mini Mental Status Examination including attentiveness, orientation, speech, language, memory and high intellectual function, Cranial nerve assessment, Reflex activity, Sensory system assessment, Motor system assessment.^[1]

Cranial nerve assessment

Cranial nerves are the nerves that emerge directly from the brain (Including the brainstem), of which there are conventionally considered twelve pairs. Cranial nerves relay information between the brain and parts of the body, primarily to and from regions of the head and neck,

including the special senses of vision, taste, smell, and hearing. The cranial nerves emerge from the central nervous system above the level of the first vertebra of the vertebral column. Each cranial nerve is paired and is present on both sides. There are conventionally twelve pairs of cranial nerves, which are described with Roman numerals I–XII. Some considered there to be thirteen pairs of cranial nerves, including the non-paired cranial nerve zero. The numbering of the cranial nerves is based on the order in which they emerge from the brain and brainstem, from front to back. The cranial nerve exam is a type of neurological examination. It is used to identify problems with the cranial nerves by physical examination. It has nine components. Each test is designed to assess the status of one or more of the twelve cranial nerves (I–XII). These components correspond to testing the sense of smell (I), visual fields and acuity (II), eye movements (III, IV, VI) and pupils (III, sympathetic and parasympathetic), sensory function of face (V), strength of facial (VII) and shoulder girdle muscles (XI), hearing and balance (VIII, VIII), taste (VII, IX, X), pharyngeal movement and reflex (IX, X), tongue movements (XII).

Olfactory Nerve (CN I)

As the name implies, the olfactory nerve serves the sense of olfaction or smell. Its fibres arise in the mucous membranes of the nose and pass through the cribriform plate of the ethmoid bone to synapse in the olfactory bulb. From here, the olfactory tract follows the ventral surface of the frontal lobe and ends in the olfactory trigone. The olfactory tract lies in the olfactory sulcus on the orbital surface of the frontal lobe. Most axons follow the lateral olfactory stria and end in the pyriform cortex (uncus, entorhinal area, and limen insulae). The medial olfactory striae terminate in the anterior olfactory nucleus and in the region of the anterior perforated substance. Olfaction is the only sensation not directly connected to the thalamus. It is important to note that the true neural networks subserving olfaction are probably much more complex as olfaction is closely integrated with memory, emotions and alimentary pleasures.

Examination

Testing of olfaction is often overlooked in clinical examination. Anosmia can be the only localizing sign of lesions in base-frontal areas compromising the olfactory pathways. It should be noted that anosmic patients do not always complain about loss of smell, but rather about altered taste. The clinical examination begins with assessing the external appearance of the nose to look for any obvious deformity. One nostril should be occluded to facilitate separate testing of each side. While a range of products can be used for testing, it is more practical to use commonly accessible items such as coffee, orange peel, vanilla etc. Noxious stimuli are detected by sensory fibres of the trigeminal nerve and pungent smells are best avoided. If anosmia is detected, an examination of the nasal passages should be considered to rule out nasal polyps and mucosal thickening. Common causes of anosmia include respiratory tract infection, increasing age, head injury, olfactory groove meningioma and following meningitis.

Optic Nerve (CN II)

This is a purely sensory nerve. It is a unique fibre pathway and not a peripheral nerve and it connects the retina to the brain. The first order neurons are activated by the rods and cones in the retina, the true peripheral nerves in this instance. These bipolar cells synapse with ganglion cells, which converge to the optic disc and form the optic nerve. Each optic nerve passes through the optic canal and joins its counterpart to form the chiasm. The spatial orientation of fibres from different parts of the fundi is preserved so that fibres from the lower part of the retina are found in the inferior part of the chiasm and vice versa. Of note, the papillomacular bundle, which originates in the peripheral portions of the optic nerve located slightly inferior and lateral, becomes more centrally located at the level of the chiasm. Fibres from the temporal visual field cross over at the chiasm but fibres from the nasal fields do not. From the chiasm the optic tract reaches three destinations: (1) the lateral geniculate body for relay to the visual cortex in the

occipital cortex; (2) pretectal nuclei for papillary reflexes to light; and (3) the superior colliculi for body reflexes to light. The optic radiation from the lateral geniculate body divides before reaching the visual cortex. The fibre tracts that originate from the upper retinal quadrants pass through the internal capsule and course within the parietal and occipital lobes to terminate on the cuneus. The lower retinal fibres pass through the internal capsule and sweep around the temporal horn of the lateral ventricle forming Meyer's loop, eventually terminating in the lingual gyrus.

Examination

Each eye should be tested separately in assessments of visual acuity, visual fields, and fundoscopy. Visual acuity. As refractory errors are not part of cranial nerve examination, the patient should use any optical aids to which they are accustomed. A hand-held eye chart or a Snellen chart can be used. During the examination, one eye should be completely covered with a small card. The examiner should be mindful that patients with impaired vision may tend to turn their head, thus inadvertently looking with the covered eye. Depending on the Snellen chart used, the patient should be tested at a distance of 20 feet (6 m) or 10 feet (3 m). The patient is asked to read progressively smaller letters until consistent perception is no longer possible. In a patient who has uncorrected visual acuity of less than 20/20 (6/6) vision, the pinhole test can be performed using a piece of cardboard with a tiny (2 mm) perforation. Improved vision indicates refractory error. If a patient is unable to read the largest letters on the chart, he or she should be asked to count fingers held up in front of them. Failing this, recognition of hand movement is tested. In cases of severe visual impairment, light perception should be tested using a pen torch. Visual fields. Visual fields can be examined by confrontation using the examiner's finger or coloured pen, but a red pen allows a more detailed assessment to be made. Using a wagging finger can reduce the sensitivity of the test in the peripheral field and can fail entirely to assess the central fields (Fig. 1). The examiner should ensure that his/her line of sight is level with that of the patient. The patient is instructed to look directly at the examiner's eye while the non-tested eye remains covered with a piece of cardboard (or the patient's hand). The red pen should be brought in from four directions diagonally towards the centre of the visual field. The patient should state when the coloured pen becomes clearly detectable. As this examination relies on comparative evaluation, the examiner should ensure that the red pen is always equidistant from each individual. An enlarged blind spot can also be mapped by asking about disappearance of the pen around the centre of the field of vision, but this can be more challenging to test.

Fundoscopy

Fundoscopy examination is performed using the ophthalmoscope to assess the optic disc and retina while the patient is looking into the distance. Regular practice

is required to achieve competence, particularly when examining patients with undiluted pupils.

Oculomotor, Trochlear, and Abducens Nerves (CN III, IV, and VI)

Cranial nerves III, IV, and VI provide motor innervations to extra-ocular muscles. The oculomotor nucleus is situated in the periaqueductal Gray at the level of the superior colliculus. The oculomotor nerve provides somatic motor inputs to all the extra-ocular muscles except the lateral rectus (abducens nerve) and superior oblique (trochlear nerve). Pupil size depends on a balance between sympathetic (mydriasis) and parasympathetic (miosis) tone. The parasympathetic innervation is through the Edinger Westphal nucleus located dorsal to CN III. Preganglionic parasympathetic fibres travel to the ciliary ganglion where postganglionic fibres relay to the pupil and ciliary muscle. Sympathetic innervation to the eyes travels from the hypothalamus via the ciliospinal centre in the spinal cord at C8, T1, and T2 to the superior cervical ganglion in the neck. From here the sympathetic fibres travel with the internal carotid artery into the cavernous sympathetic plexus. This in turn travels within the ophthalmic division of the trigeminal nerve to innervate the eye through the long and short ciliary nerves. Of note, the sympathetic plexus also innervates the tarsal muscles and the orbital muscle of Muller. The trochlear nerve (CN IV) is located immediately beneath and lateral to the oculomotor nerve in the mesencephalon. The fibres decussate in the anterior medullary velum of the aqueduct of Sylvius. They then travel forward to pierce the dura, which forms the lateral wall of the cavernous sinus, below the oculomotor nerve. The abducens nerve (CN VI) arises from the pons ventral to the fourth ventricle. Its fibres emerge ventrally between the pons and medulla, and then ascend between the pons and the clivus. Dorello's canal channels the nerve towards the cavernous sinus where the nerve courses in close proximity to the carotid artery.

Examination

Pupils. The size, shape, and symmetry of pupils should be noted on inspection. An irregular pupil can suggest previous surgery or traumatic injury. Direct and indirect pupillary responses to light should be elicited. The direct response is the constriction that occurs when the pupil is exposed to light. The consensual or indirect response refers to the simultaneous constriction of the opposite pupil. The torch should be moved in an arc from pupil to pupil to assess for an afferent pupillary defect. This is also known as the Marcus Gunn sign, where the affected pupil dilates paradoxically after a short time when the light source is moved from a normal to an abnormal eye. The light reflex and resting pupil size are dependent on light perception by at least one eye. If both eyes are blind owing to a lesion anterior to the lateral geniculate bodies, both pupils will be fixed and nonreactive to light. If blindness is secondary to destruction of the visual cortex the light reflex will be preserved. Accommodation refers to the pupillary constriction that occurs as the patient

attempts to converge his or her eyes. To test this, the patient is initially asked to look into the far distance and then asked to focus on the tip of his or her nose. Causes of an absent light reflex with an intact accommodation reflex include a midbrain lesion or a ciliary ganglion lesion. In very rare cases, failure of accommodation only can occur after a midbrain lesion or cortical blindness.

Eye movements

Failure of movement, diplopia and nystagmus are assessed in this examination. The examiner should be 30–40 cm in front of the patient and a hat pin should be moved in an “H” pattern. Patients should be asked to follow the target with their eyes without moving their heads. Look for failure of movement and ask about diplopia. If any abnormality is detected, each eye should be tested individually. Diplopia is an early sign of extraocular muscle weakness. The false image is usually paler, less distinct and more peripheral. The patient should be asked if the images are side by side or one above the other. A side-by-side position indicates only the lateral and medial recti are involved. To assess the muscles involved, the direction in which image separation is maximal should be established. Image separation is greatest in the direction of the purest muscle action of the weak muscle. At the point of maximal image separation, cover one eye. Disappearance of the false image indicates that the covered eye is responsible.

Trigeminal Nerve (CN V)

The trigeminal nerve is the largest cranial nerve and has both sensory and motor fibres. It emerges from the pons and runs within the cerebellopontine angle. At the petrous temporal bone, it forms the trigeminal ganglion housed within Meckel's cave. The trigeminal ganglion gives rise to three divisions. The ophthalmic division (V1) runs within the lateral wall of the cavernous sinus to enter the orbital fissure superior to supply the skin of the forehead and the cornea and conjunctiva. The maxillary division (V2) supplies the skin in the middle of the face, mucous membranes in the upper part of the mouth palate and the nasopharynx. The mandibular division (V3) runs with the motor part of the nerve and leaves the skull through the foramen ovale to supply the skin of the lower jaw and muscles of mastication (temporalis, masseter, pterygoids).

Examination

The three trigeminal divisions are tested using a cotton wool ball and blunt tip needle sequentially on the forehead, malar eminence and lower face over the mandible, while comparing sides. Loss of pain sensation will result in the pin prick feeling dull. The area of dullness should be mapped. Light touch can be tested with cotton wool, but temperature is rarely tested except in syringobulbia. Corneal reflex testing is simple to perform but potential problems must be recognized. The assessor should ideally be positioned to the side or behind the patient to avoid a blink reflex, which can be triggered by sudden movements in the patient's visual

field. A wisp of cotton is used to touch the cornea gently while the patient is gazing towards the distance. The examiner should ask if the patient felt the corneal contact and look for blinking in both eyes. Reflex blinking of both eyes is a normal response. If blinking occurs only in the contralateral eye, this can indicate ipsilateral seventh nerve palsy. The motor component of the trigeminal nerve can be assessed by examining the function of the temporalis, masseteric and pterygoid muscles. With the patient clenching, the temporalis and masseteric muscles are palpated to assess for tone and muscle bulk. The strength of these muscles can be tested by asking the patient to bite on a wooden tongue depressor. The depth of the bite marks can be used to assess muscle strength. The patient can also be asked to hold the mouth open while the examiner attempts to force it shut. This test assesses the strength of the pterygoid muscles. An exaggerated jaw reflex can be a valuable sign indicating an upper motor neuron lesion. After an index finger is placed on the chin and a tap with the tendon hammer elicits any reflex. Normally there is slight closure of the mouth or no reflex at all.

Facial Nerve (CN VII)

The facial nerve is predominantly a motor nerve with parasympathetic and sensory components. The sensory division is separate from the motor division and is sometimes referred to as the “nervus intermedius.” The motor nucleus is located ventral and medial to the abducens nucleus in the pons. The fibers then loop around the abducens nucleus before exiting the Ponto-medullary junction with the eighth cranial nerve to enter the internal acoustic meatus above the eighth nerve. After entering the facial canal, the nerve enlarges to become the geniculate ganglion. The corda tympani, which contain the taste fibers from the anterior two thirds of the tongue, join the nerve in the facial canal. The facial nerve exits the skull at the stylomastoid foramen and divides into its terminal branches within the parotid gland to supply the muscles of facial expression. The efferent parasympathetic fibers initiate salivation, lacrimation and mucous membrane secretion. These fibers travel in the corda tympani nerve to supply the submandibular, submaxillary, and lacrimal glands.

Examination

The facial nerve provides innervation for the muscles of facial expression. Close observation of a patient's face can yield the initial clues of asymmetrical expression (e.g., flattening of the nasolabial groove) in a patient with facial nerve palsy. The upper part of the face is relatively spared in facial paresis of an upper motor neuron pattern owing to bilateral cortical representation. This can be tested by instructing the patient to look upwards, which can exaggerate the wrinkling the forehead. Next, the patient should be asked to close both eyes tightly while the examiner attempts to force open each eye to test strength. To assess the muscles of expression in the lower face, the patient is asked to show his/her teeth and to “puff out” the cheeks, and then the

cheeks are palpated to determine any difference in tone. A lower motor neuron lesion results in paresis/paralysis of all the ipsilateral facial muscles. Unilateral upper motor neuron facial nerve paresis can commonly result from vascular lesions or tumors. A lower motor neuron pattern of facial paresis is seen in Bell's palsy, multiple sclerosis and tumors (e.g., meningiomas and vestibular schwannomas) that compress the facial nerve. Bilateral facial nerve weakness is uncommon. Causes include Guillain–Barre syndrome, sarcoidosis and bilateral parotid disease.

Vestibulocochlear Nerve (CN VIII)

This nerve is sensory, specialized for sound reception and balance. Fibers for hearing originate in the hair cells of the organ of Corti. They travel towards the bipolar cells of the spiral ganglion within the cochlea. The nerve emerges from the cochlea and passes through the internal acoustic meatus to enter the upper medulla at its junction with the pons. The fibers terminate in the cochlear nuclei located in the pons. Fibers for balance originate in the maculae of the utricle and saccule and the cristae of the ampullae of the semicircular canals. Impulses travel to the bipolar cells of Scarpa's ganglion. The vestibular nerve emerges through the internal auditory meatus to join the auditory fibers in the facial canal. The nerve eventually enters the brainstem at the Ponto-medullary junction and relays in the vestibular nuclei. Examination Auditory. Hearing. Test one ear at a time. A simple test would involve blocking the contralateral ear with a finger and whispering numbers in the ipsilateral ear. Numbers such as 68 can be used to test for high tone and 100 for low tone. Whispering should be performed at the end of respiration at distance of 60 cm to standardize the examination. If any deficits are noted, Rinne's and Weber's tests are performed. Rinne's test. A 256 Hz tuning fork is struck and placed on the mastoid process. The patient is requested to indicate when the sound is no longer audible. As soon as the sound is extinguished, the tuning fork is placed next to the external auditory meatus to assess whether it can be heard. In a patient with normal hearing, air conduction should be greater than bone conduction, so the patient should be able to hear the tuning fork next to the ear after it is no longer audible against the mastoid. With conductive deafness, the patient will not be able to hear the tuning fork when it is moved next to the external auditory meatus. In sensorineural deafness, the mastoid and external auditory meatus components are equally reduced. Weber's test. A 256-Hz tuning fork is placed in the middle of the forehead and the sound is heard from there. In sensorineural deafness the sound is heard better in the normal ear. A patient with conduction deafness finds the sound louder in the abnormal ear. Vestibular system. A bedside examination of the vestibular system is difficult to perform. This system can be assessed indirectly, without performing specialized tests such as Hallpike's maneuver, by assessing the patient's gait and looking for nystagmus.

Glossopharyngeal Nerve (CN IX)

As the name implies, this nerve originates from the medulla and innervates primarily the muscles of the tongue and pharynx. The nerve emerges from the medulla as three to six rootlets between the inferior olive and the inferior cerebellar peduncle. It exits through the jugular foramen within a separate dural sheath (lateral and anterior to CNs X and XI). The glossopharyngeal nerve then travels within the carotid sheath and ultimately terminates in the lateral pharyngeal wall. The nerve provides both sensory and motor innervations to structures in the glossopharynx. Efferent nerves innervate the stylopharyngeus muscle. Autonomic fibers supply the parotid gland and mucous membranes of the posterior inferior mouth and membranes through the tympanic nerve (Jacobson's nerve). Afferent fibers arise from the retro auricular region with tactile, thermal and noxious stimuli from the mucous membranes of the posterior third of the tongue, the tonsils, and the Eustachian tube. Taste sensation is carried from the posterior tongue region. Hering's nerve, a special visceral afferent nerve, arises just below the jugular foramen. It innervates the carotid sinus and body and brings chemo- and baro-receptor inputs to the medulla. Together with collateral inputs via the vagal nerve, the glossopharyngeal-vagal reflex slows the heart rate or lowers blood pressure.

Examination

Clinical examination of the glossopharyngeal nerve is typically performed in conjunction with the vagus nerve, as separate testing is challenging. A unilateral lesion in the glossopharyngeal nerve can manifest as loss of the ipsilateral gag reflex, carotid body and sinus reflex and taste in the posterior region of the tongue. In practice, only the gag reflex is assessed. The examiner should explain the procedure thoroughly and state that it may be uncomfortable, so that the patient knows what is to be expected prior to testing. With a tongue depressor, the back of the throat is touched gently on one side. This normally triggers the gag reflex. If this is weakened or absent, the patient should be asked if the sensation was felt equally on both sides.

Vagus Nerve (CN X)

The vagus nerve also originates in the medulla and innervates multiple structures. The Latin root of its name translates as "wandering," reflecting its long and wide distribution. The nerve exits just below the glossopharyngeal nerve in the medulla. It courses towards the jugular foramen, posterior and medial to CN IX, then travels down in the carotid sheath. Like the glossopharyngeal nerve, this nerve contains both afferent and efferent projections. The efferent innervations convey general visceral efferents to the thorax, abdominal viscera, and muscles of the pharynx and larynx. Afferents arise from the external ear, external auditory canal, surface of the tympanic membrane, pharynx, larynx, trachea, esophagus and viscera of the thorax and abdomen.

Examination

The vagus nerve is typically evaluated in conjunction with the glossopharyngeal nerve. The examiner should take note of the patient's voice during conversation. An isolated recurrent laryngeal nerve (branch of the vagus nerve) palsy results in a hoarse voice. When the patient is asked to cough, the failure of vocal cord closure produces a hollow "bovine" sound. Unilateral vagus nerve lesions result in hoarseness, dysphagia and dyspnea secondary to loss of branchiomeric muscle innervations. While testing the gag reflex, the examiner should note the position of the uvula and look for symmetrical elevation of the soft palate to exclude uvular deviation away from the side of the vagus nerve lesion. A simple bedside swallowing assessment can also be performed by asking the patient to drink small sips of water. Patients with bulbar palsy can be at risk of aspiration. Bilateral vagal nerve injuries are usually fatal owing to laryngeal paralysis, which results in airway obstruction and asphyxia.

Spinal Accessory Nerve (CN XI)

The spinal accessory nerve is formed from cranial and spinal contributions. The spinal roots arise from the ventral horn cells in the cord from C1-C5 and travel cranially through the foramen magnum. These fibers travel in turn to the clivus, turning laterally towards and then exiting through the jugular foramen after joining the cranial portion discussed above. The spinal portion of the nerve innervates the sternocleidomastoid and upper part of the trapezius through somato-motor fibers. The cranial portion communicates with the jugular ganglion of the vagus nerve, and innervates the intrinsic muscles of the pharynx through the recurrent laryngeal nerve branch.

Examination

A lesion or injury to the cranial portion of the spinal accessory nerve is difficult to distinguish from one of the vagal nerve, as described above. Hence, clinical examination focuses on the bulky muscles innervated by the spinal portion of the nerve. The tone and bulk of the sternocleidomastoid and trapezius muscles are initially examined by close observation and palpation. The trapezius is tested by asking the patient to shrug their shoulders while applying resistance. In severe cases of ipsilateral trapezius muscle atrophy, shoulder sag with downward and outward rotation of the scapula can be observed. The sternocleidomastoid is assessed by asking the patient to turn his/her head against resistance applied to the side of the face. In cases of unilateral palsy, the patient is unable to turn the head to the side opposite the lesion as the sternocleidomastoid muscle is weak.

Hypoglossal Nerve (CN XII)

The hypoglossal nerve provides motor innervation to the tongue musculature. The hypoglossal nucleus resides primarily in the medulla oblongata. The exiting fibers emerge from a sulcus between the pyramid and inferior olive. The nerve then enters the hypoglossal canal and

exits towards the angle of the mandible. It subsequently courses anteriorly to supply both the intrinsic and extrinsic tongue muscles.

Examination

The tongue is carefully inspected for signs of atrophy and asymmetry. With atrophy the tongue starts to lose its bulk at the tip and the border area. This progresses until it appears wrinkled. The patient is then asked to protrude the tongue; there is tongue deviation towards the side of the lesion in pathological conditions. Fasciculations may be seen in patients with motor neuron disease (amyotrophic lateral sclerosis). While the tongue is at rest, fasciculations usually persist while resting tremors abate. Power is examined by having the patient press the tip of the tongue against each cheek while the examiner tries to dislodge it. With facial weakness, tongue deviation can appear to be produced when none is present. Hence, manual elevation of the weak side of the face can be helpful in eliminating this finding.^[2]

Mini mental status examination

A Mental Status Examination (MSE) is a structured assessment of an individual's current cognitive and emotional functioning. It involves observing and evaluating various aspects of a person's mental state during a clinical interview. Here are some key components typically included in an MSE.

Appearance and Behaviour – Observation of physical appearance, grooming, and any unusual behaviours or movements.

Speech and Language – Assessment of speech rate, volume, coherence, and any abnormalities such as stammering or slurring.

Mood and Affect – Mood refers to the predominant emotional state (e.g., sad, euphoric, anxious). Affect describes the emotional expression observed (e.g., flat, blunted, appropriate).

Thought process – Evaluation of how thoughts are organized (e.g., logical, tangential, circumstantial) and the flow of thought.

Thought content – Exploration of the content of thoughts, including any delusions, obsessions, or preoccupations.

Perceptions – Inquiry about hallucinations or illusions (e.g., auditory, visual, tactile).

Cognition – Assessment of cognitive functions such as orientation (to time, place, person), attention, concentration, memory, and reasoning.

Insight and Judgment – Insight refers to the individual's awareness and understanding of their own condition. Judgment relates to their ability to make sound decisions and understand the consequences of their actions.

MSE findings are crucial in formulating diagnoses, determining treatment plans, and monitoring progress over time. It provides a snapshot of the person's mental state at the time of assessment, helping clinicians to understand their strengths, challenges, and needs.

provide some reference for above information.^[3]

Motor assessment

Nerve injuries can be broadly categorized as either neuromeric in which the nerve and nerve sheath are disrupted or axonometric where by the axons are damaged but the connective tissues endoneurium perineurium and epineurium remain intact. After axonotmesis or neurotmesis, the nerve will undergo Wallerian degeneration and subsequent axonal regrowth. Wallerian degeneration while necessary for regeneration is known to initiate inflammatory process. The nerve assessment algorithms have the potential to impact diagnosis interaction and recovery of impaired nerve a comprehensive view of the literature assessing their efficacy could ultimately assist surgeons in improving patient outcomes.

Methods

British medical research council (BMRC) – developed a grading system that assessed contractile muscle high score indicating greater strength. It is best suited for assuming nerve injuries of the upper arm & the upper 3rd of the forearm but less useful for aided nerve injuries.

Manual muscle testing (MMT) – MMT assess multiple domains of motor recovery & was described in the literature as easily as 1915. Used to help determine the extent of nerve injury by assigning a grade to muscle contraction.

Pinch strength test – It is commonly used to assess ulnar nerve function as it requires thumb addition. Tip-to-tip or tripod pinches can assess extent of nerve injury or recovery in the median nerve.

Muscle Dynamometer-Manner felt – The test allows for individualized action assessment such that surgeons can identify the activity of particular muscle movements, especially in ulnar nerve repair patients. Dynamometry can also measure the ability of the intrinsic & extrinsic hand muscles to work together.

Jebson-Taylor Hand function test – It is a timed test that consists of seem tasks to test fine motor, weighed & non-weighted hand functions. Means time to complete a task is recorded to assess a patient's level of hand dysfunction.

Sollerman's Grip Test – It is used to understand the quality of hand grip & to correlate that grip of hand grip & to correlate that grip write difficulty in performing a task.

Rosum and Lundborg scale – This assesses outcome of median & ulnar nerve repair via motor, sensory & pain domains. With outcomes scale is SWM & shape Identification tests for sensory states, MMT & grip strength testing for motor status & a four-point self-report scale for pain status.^[4]

Reflex activity

Reflex activity is known as reflex action is an automatic and rapid response to a specific stimulus or change in the environment. Reflex activities are mediated by the

nervous system which activates a specific set of muscle or glands in response to a particular stimulus.

Examples of reflex activity – Withdrawing a hand from a hot surface, blinking when something approaches to eyes, Knee-jerk response when the patellar tendon is tapped, Sneezing or coughing when the nasal passages or airways are irritated.

Reflex activities are important for survival and can help protect the body from harm but they can also be influenced by learning and experience.

Stretch Reflexes – Many of us know about stretch reflexes. When a physician taps the tendon near our knee cap to elicit a quick knee extension. This procedure used as diagnostic tool to determine the integrity of the spinal cord and the extension response it elicits may seem otherwise useless. Stretch reflexes are often thought to quickly resist unexpected changes in muscle length via a very simple circuit in the spinal cord and this is one circuit that the tendon tap engages. It turns out however that stretch reflexes support a myriad of functions and are highly flexible. Under naturalistic conditions stretch reflexes are shaped by peripheral physiology and engage neural circuits spanning the spinal cord, brain stem and cerebral cortex.

Cardiovascular regulation by skeletal muscle reflexes in Health and Diseases – Heart rate and blood pressure are elevated at the onset and throughout the duration of dynamic or static exercise. Mechanically sensitive and metabolically sensitive receptors activating the exercise pressor reflexes are located on the unencapsulated nerve terminals of group III group IV afferent sensory neurons respectively. The chemical by-products of muscle contraction also stimulate metaboreceptors one activated group III and group IV sensory impulse are transmitted to cardiovascular control centres within the brain stem where they are integrated and processed. Activation of the reflexes results in an increase in efferent sympathetic nerve activity and a withdrawal of parasympathetic nerve activity. These actions result in the precise alterations in cardiovascular hemodynamic requisite to meet the metabolic demands of working skeletal muscle. Coordinate activity by this reflex is altered after the development of cardiovascular disease generating exaggerated increase in sympathetic nerve activity blood pressure, heart rate, and vascular.^[5]

Literature review

Edizidni Minerva, *et al* 2020, have conducted study on “efficacy of a proprioceptive exercise program in patients with nonspecific neck pain a randomized controlled trial. The aim of his study was to compare the effectiveness of two therapeutic exercise programs in reducing pain and disability in individuals with nonspecific neck pain. Further aimed to compare the effectiveness of the two treatments in improving pressure pain in thresholds cervical range of motion and head

repositioning accuracy. The result of his study shows the improved therapeutic effects of an intervention protocol that include proprioceptive cervical exercises on pain, neck disability, ROM and HRA in people suffering from sensitivity and disability significantly improved for both interventions. Conclude that a program based on cervical proprioception exercise demonstrated to improve pain, disability, pressure pain threshold range of motion and head repositioning accuracy in patients with nonspecific pain. However, a program based on cervical mobility exercises only showed to improve pain intensity and disability, while such improvement was not clinically relevant.^[6] M.A.L shami, *et al*, 2021, have conducted study on “effect of manual therapy with exercise in patient with chronic cervical radiculopathy: a randomised clinical trial. the study was to examine the short-term effects of vertebral mobilization on the sensory features in patients with radiculopathy. In methodology, the small number of patients in the current study might not allowed subgroup analysis. Because the subgroup analysis is generally not recommended due to several issues such as emerging of false- positive results. In conclusion that the cervical vertebral mobilization for patients with chronic cervical radiculopathy reduced localized mechanical but not thermal pain hypersensitivity.^[7] Elsevier Espana, *et al* 2021, have conducted study on effects of motor imagery on strength range of physical function, pain intensity in patients with total knee arthroplasty; a systemic review and meta-analysis. The aim is to be assess the impact of MI on strength, active range of motion [ROM]. Pain intensity and physical function in patients with TKA. main aim of the present systemic review and, meta-analysis was to investigate the effects of MI on clinical outcomes in patients with TKA. our results showed that there is low certainty evidence that adding a MI intervention to standard rehabilitation may increase knee strength and reduce pain. However, it is uncertain whether MI can improve active ROM and mobility. Furthermore, our findings suggest that when MI is performed in the post-acute term it may improve active ROM. conclude that there is low to very low-quality evidence that adding an MI intervention to standard rehabilitation for patients with TKA may improve quadriceps strength and pain intensity, but the effects of motor imaginary on range of motion and physical function is unclear.^[8]

Jhonwiley, *et al* 2021, have conducted study on “Evaluation of children’s pain expression and behaviour using audio visual distraction. dental anxiety distress children and their families with consequent poor and oral health and costly paediatric dental services. children’s behaviour could be modified using a distraction technique for improved dental treatment. The study evaluates the effects of an audio-visual distraction on children’s behaviour and pain expressions during dental treatment. Conclude that AVD is an effective distraction tool for young children during dental treatment regardless of child’s subjective pain expression.^[9] Rachels-Hayward, *et al* 2021, have conducted study on

effect of intramuscular injection technique on injection associated pain; a systematic review and meta-analysis. The aim is to review the effect of different intramuscular injection [IMI] techniques on injection associated pain in adults. We identified a variety of IMI technique which reduces injection site pain among diverse patients' groups and health care settings. we found some evidence supporting the use of manual pressure at the site of injection. post injection massage was found to be beneficial in reducing injection pain in a single unblinded, quasi-experimental study of 30 participants but further larger studies are required to confirm any benefit. They conclude manual pressure or rhythmic tapping over the injection site and applying local pressure around the injection site reduced IMI pain. however, there was very high unexplained heterogeneity between studies and risk of significant bias within small studies.^[10] Jill A Hayden *et al*, 2021, Have conducted a network meta-analysis on "Some types of exercise are more effective than others in people with chronic low back pain: Network Meta Analysis" and it reveals that most exercise types were more effective than minimal treatment for pain and functional limitation outcomes and results were compatible with moderate to clinically important treatment effects for Pilates, MC Kenzie therapy and functional restoration (pain only) and flexibility exercises and the review found evidence that Pilates, MC Kinzie therapy and functional restorations were more effective than other types of exercises treatment for reducing Pain.^[12] Osama M. Felemban, 2021, have conducted a randomised clinical trial on "Effect of visual reality distraction on pain and anxiety during infiltration anaesthesia in paediatric patients" and the clinical trial reveals that healthy 6-12 years children and women are administered local anaesthetic and children are administered while watching a cartoon. To assess anxiety heart rate is recorded. As a result, the female subjects and younger age group were more likely to report highest pain scores during local anaesthesia administration.^[13]

Mario Romero- Palau *et al*, 2021 have conducted a systematic review and meta-analysis on "Effect of motor imaginary on strength, range of motion, physical function, and Pain intensity in patients with total Knee arthroplasty". and it reveals that the positive effect of motor imaginary in restoring quadriceps strength, active Rom, and decrease pain intensity in patients after TKA. There is low evidence that adding motor imaginary to a standard rehabilitation programme for patients with TKA likely improve quadriceps strength and decreases pain intensity but not physical function.^[14] Huga Jario Almeida silver *et al*, 2021 have conducted a randomised trial on "Dry cupping therapy is not superior to sham cupping to improve clinical outcomes in people with non-specific chronic low back pain", and it reveals that the experimental group received dry cupping therapy and control group received sham cupping therapy. the interventions were applied once a week for 8 weeks. participants were assessed before and after treatment and

outcomes were pain intensity, physical function, functional mobility, quality of life, similarly negligible effects were observed and by this we can conclude that dry cupping therapy is not superior to sham cupping in people with non-specific chronic low back pain.^[15]

Antonio Maniaci *et al*, 2021, have conducted a systemic review and meta-analysis on "Endoscopic surgical treatment for rhinogenic contact point headache" and it reveals that surgical treatment in patients with Shino genic contact points exhibited significantly better values. surgical treatment demonstrated significantly better post-operative scores than medical treatment.^[16] Jones G, *et al*, 2022, January, have conducted study on "The efficacy and safety of transcutaneous electrical nerve stimulation [TENS] for acute and chronic pain in adults; a systematic review and meta-analysis of 381 studies". They study to investigate the efficacy and safety of transcutaneous electrical nerve stimulation [TENS] for relief pain in adult. In methodology randomised control trials [RCT] comparing strong non-painful placebo or other treatments in adults with pain, irrespective of diagnosis. In conclusion there was moderate-certainly evidence that pain intensity was lower during or immediately after TENS compared with placebo and serious adverse events.^[17] Andrew H. Rogers *et al*, 2022, have conducted study on "A meta-analysis of the association of elements of the fear avoidance model of chronic pain with negative affect, depression, anxiety, pain-related disability and pain intensity". They study aimed to provide a comprehensive analysis of the magnitude of the cross-sectional association between the primary components of the fear-avoidance model with negative effect anxiety, depression, pain intensity and disability in studies of clinical pain. In conclusion these findings provide empirical support, aligned with the components of the fear-avoidance [FA] model for the relevance of both pain catastrophizing and fear of pain-to-pain experience and its intersection with mental health.^[18]

Tumer *et al*, 2022, have conducted study on "Behavioural activation and behavioural inhibition: An examination of function in chronic pain "The study to examine the BIS- BAS model of chronic pain. This model posits those two neurophysiological systems – the behavioural inhibition system [BIS] sensitized to and activated by punishment cues and the behavioural activation system [BAS] sensitized to and activated by reward cues. In conclusion BIS and BAS both contribute to pain-related functions. Both relationships would differ based upon the nature of the functional outcome. BIS resulting in poorer function due to pain and BAS better function despite pain may be more pervasive across functional outcomes.^[19] Bruno Dubois *et al*, 2023, have conducted a clinical trial on "Masitinib For mild-to-moderate Alzheimer's disease-results from a randomized, placebo controlled, phase 3, Clinical trial" & found that masitinib (4.5mg/kg/day) showed significant benefit over placebo according to the primary end Point of ADAS-Cog, - 1.46 versus 0.69, respectively,

with a significant between group difference was of -2.15; $P < 0.001$. For the ADCS-ADL primary end point, the between group difference was 1.82 versus -0.81.^[20] Aline Mendonca Turci *et al.*, 2023, have conducted randomised trial on "Self-administered stretching exercises are as effective as motor control exercises for people with Chronic non-specific low back pain: A randomized trial". They found out that in people with chronic non-specific low back pain, self-stretching exercises had very similar effects to motor control exercises on pain intensity, disability, Fear avoidance, global Perceived effect & flexibility up to 18 weeks beyond the end of 8-week Program. The chance of intervention might be directed by Patient Preference.^[21] Zhengze Yu *et al.*, 2023, have conducted a "Study on efficacy of Pilates on Pain, functional disorders & Quality of life in Patients with Chronic low back Pain: A systemic review & Meta-Analysis" and the meta-analysis reveals that Pilates may have Positive efficacy for Pain relief & the improvement of functional disorders in CLBP patients, but the improvement in quality of life seems to be less obvious.^[22] Shahul Hameed Pakkir Mohamed *et al.*, 2023, have conducted clinical trial on "Effectiveness of Kinesio taping and Conventional Physical therapy in the management of knee osteoarthritis" and found out that Kinesio taping combined with Conventional Physical therapy was found to be more effective than Conventional Physical therapy alone in the third and Sixth weeks of the treatment. In knee Osteoarthritis of treatment was found to reduce Pain, enhance range of motion, and improve physical functioning.^[23]

Er & Yuksel *et al.*, 2023, have conducted study on "A Comparison of the effect of connective tissue massage & classical massage on chronic mechanical low back Pain" & showed that massages were similar effect. The fact that Classical massage is a frequently used technique in pain management & is an effective as Connective tissue massage in Automatic responses will make it more Preferred in the clinic.^[24] Lawrence S. Honig *et al.*, 2024, have conducted a study on "Updated safety results from phase 3 lecanemab study in early Alzheimer's disease". Clarity Alzheimer's disease was an 18-month treatment, multicentred, double-blind, placebo-controlled, parallel-group study with open-label extension in Participants with early Alzheimer's diseases. Eligible Participants were randomized 1:1 across 2 treatment groups. Lecanemab was generally well-tolerated, with the most common adverse events being infusion-related reactions. ARIA-H, ARIA-E. Clinicians, participants & Caregivers should understand the incidence, monitoring management of these events for optimal Patient care.^[25] Naruhiko Sahara and Makoto, Higuchi *et al.*, 2024, have conducted a study on 'Diagnostic and therapeutic targeting of Pathological tau proteins in neurodegenerative disorders. The tau protein belongs to the family of Tau/MAP2/MAP4 microtubule-associated proteins. In the CNS tau is mostly expressed in neurons but is also present at low levels in glia. Tau PET imaging

also holds the Potential for diagnosing tauopathies by evaluating the distribution of Pathological tau deposits in living brains. Additionally, interventions in protein degradation, systems such as the UPS & autophagy-lysosome system, as well as microglial phagocytosis, are currently being investigated for their effectiveness as disease-modifying therapies.^[26] L. Salvesen *et al.*, 2024 have conducted study on "influencing dreams through sensory stimulation. They found that sleep the changes dream frequency or content are commonly report symptoms of primary sleep disorders including insomnia and parasomnias and psychiatric and neurologic disease. The study concluded that the utilization of sensory stimulation is particularly relevant among the various dream engineering techniques due to its reliance on well-established physiological pathways and function case of implementation and extension history of anecdotal and empirical observation.^[27] Rubega M. *et al.*, 2024 have conducted study on Neurological, balance and motion evidence in adolescent idiopathic scoliosis they aimed to summarise the neurophysiological balance and motion evidence related to both observational and interventional studies were considered. They study concluded this review underscores the importance of quantitative assessment methods to explore the etiology and pathophysiology of AIS. Wang *et al.*, 2024 have conducted study on effect of acupuncture combined with rehabilitation training on sensory impairment of patients with stroke. They study aimed to compare the effect of different acupuncture related treatment combined with rehabilitation training on sensory impairment and the daily living ability of patients with stroke the study concluded that the combinational of acupuncture related treatment and modern rehabilitation training not only improve the symptoms of sensory impairment and numbness after stroke but also enhance the daily of patients especially when acupuncture is combined with rehabilitation.^[28] Yangquan Ni, *et al.*, 2024 have conducted study on efficacy of sensory based static balance training on the balance ability aging attitude and perceived stress of older adults in the community. A randomized controlled trial. This study explores the effect of sensory based static balance training on the balance ability aging attitude and perceived stress of older adults in community. In methodology A totally of 72 older adults were recruited and randomly divided into an interventional group and control group balance ability aging attitude and perceived stress were assessed at baseline and 12- 24 weeks repeated measure ANOVA and generalized estimated equations were used to compare outcome measures.^[29]

CONCLUSION

The neurological examination remains an indispensable tool in the diagnosis and management of neurological disorders, bridging clinical acumen with technological advancements. While traditional techniques such as reflex testing, sensory assessments, and cranial nerve evaluations continue to provide critical diagnostic insights, the integration of modern innovations, including

neuroimaging, digital tools, and artificial intelligence, has significantly enhanced accuracy and efficiency. This literature review underscores the need for a balanced approach, combining time honoured methods with emerging technologies to ensure comprehensive patient care. Future research should focus on refining diagnostic algorithms, improving accessibility, and leveraging cutting-edge tools to further optimize neurological assessments, paving the way for more personalized and effective treatment strategies.

REFERENCES

1. Suzuki Y, Iijima H, Tashiro Y, Kajiwara Y, Zeidan H, Shimoura K, Nishida Y, Bito T, Nakai K, Tatsumi M, Yoshimi S, Tsuboyama T, Aoyama T. Home exercise therapy to improve muscle strength and joint flexibility effectively treats pre-radiographic knee OA in community-dwelling elderly: a randomized controlled trial. *Clin Rheumatol*, 2019; 38(1): 133-141. doi: 10.1007/s10067-018-4263-3. Epub 2018 Aug 30. PMID: 30167975; PMCID: PMC6342874.
2. Chen H, Zheng X, Huang H, Liu C, Wan Q, Shang S. The effects of a home-based exercise intervention on elderly patients with knee osteoarthritis: a quasi-experimental study. *BMC Musculoskelet Disord*, 2019; 9, 20(1): 160. doi: 10.1186/s12891-019-2521-4. PMID: 30967131; PMCID: PMC6456993.
3. Karasawa Y, Yamada K, Iseki M, Yamaguchi M, Murakami Y, Tamagawa T, Kadowaki F, Hamaoka S, Ishii T, Kawai A, Shinohara H, Yamaguchi K, Inada E. Association between change in self-efficacy and reduction in disability among patients with chronic pain. *PLoS One*, 2019; 16, 14(4): e0215404. doi: 10.1371/journal.pone.0215404. PMID: 30990842; PMCID: PMC6467389.
4. Elboim-Gabyzon M, Andrawus Najjar S, Shtarker H. Effects of transcutaneous electrical nerve stimulation (TENS) on acute postoperative pain intensity and mobility after hip fracture: A double-blinded, randomized trial. *Clin Interv Aging*, 2019; 29, 14: 1841-1850. doi: 10.2147/CIA.S203658. PMID: 31754300; PMCID: PMC6825510.
5. Zou L, Zhang Y, Liu Y, Tian X, Xiao T, Liu X, Yeung AS, Liu J, Wang X, Yang Q. The Effects of Tai Chi Chuan Versus Core Stability Training on Lower-Limb Neuromuscular Function in Aging Individuals with Non-Specific Chronic Lower Back Pain. *Medicina (Kaunas)*, 2019; 3, 55(3): 60. doi: 10.3390/medicina55030060. PMID: 30832454; PMCID: PMC6473361.
6. Espí-López GV, Aguilar-Rodríguez M, Zarzoso M, Serra-Añó P, Martínez DE LA Fuente JM, Inglés M, Marques-Sule E. Efficacy of a proprioceptive exercise program in patients with nonspecific neck pain: a randomized controlled trial. *Eur J Phys Rehabil Med*, 2021; 57(3): 397-405. doi: 10.23736/S1973-9087.20.06302-9. Epub 2020 Oct 13. PMID: 33047944.
7. Alshami AM, Bamhair DA. Effect of manual therapy with exercise in patients with chronic cervical radiculopathy: a randomized clinical trial. *Trials*, 2021; 18, 22(1): 716. doi: 10.1186/s13063-021-05690-y. PMID: 34663421; PMCID: PMC8525034.
8. Ferrer-Peña R, Cuenca-Martínez F, Romero-Palau M, Flores-Román LM, Arce-Vázquez P, Varangot-Reille C, Suso-Martí L. Effects of motor imagery on strength, range of motion, physical function, and pain intensity in patients with total knee arthroplasty: A systematic review and meta-analysis. *Braz J Phys Ther*, 2021; 25(6): 698-708. doi: 10.1016/j.bjpt.2021.11.001. Epub 2021 Nov 30. PMID: 34872869; PMCID: PMC8721059.
9. Delgado A, Ok SM, Ho D, Lynd T, Cheon K. Evaluation of children's pain expression and behavior using audio visual distraction. *Clin Exp Dent Res*, 2021; 7(5): 795-802. doi: 10.1002/cre2.407. Epub 2021 Feb 23. PMID: 33622030; PMCID: PMC8543459.
10. Ayinde O, Hayward RS, Ross JDC. The effect of intramuscular injection technique on injection associated pain; a systematic review and meta-analysis. *PLoS One*, 2021; 3, 16(5): e0250883. doi: 10.1371/journal.pone.0250883. PMID: 33939726; PMCID: PMC8092782.
11. Hayden JA, Ellis J, Ogilvie R, Stewart SA, Bagg MK, Stanojevic S, Yamato TP, Saragiotto BT. Some types of exercise are more effective than others in people with chronic low back pain: a network meta-analysis. *J Physiother*, 2021; 67(4): 252-262. doi: 10.1016/j.jphys.2021.09.004. Epub 2021 Sep 16. PMID: 34538747.
12. Felemban OM, Alshamrani RM, Aljeddawi DH, Bagher SM. Effect of virtual reality distraction on pain and anxiety during infiltration anesthesia in pediatric patients: a randomized clinical trial. *BMC Oral Health*, 2021; 25, 21(1): 321. doi: 10.1186/s12903-021-01678-x. PMID: 34172032; PMCID: PMC8234622.
13. Ferrer-Peña R, Cuenca-Martínez F, Romero-Palau M, Flores-Román LM, Arce-Vázquez P, Varangot-Reille C, Suso-Martí L. Effects of motor imagery on strength, range of motion, physical function, and pain intensity in patients with total knee arthroplasty: A systematic review and meta-analysis. *Braz J Phys Ther*, 2021; 25(6): 698-708. doi: 10.1016/j.bjpt.2021.11.001. Epub 2021 Nov 30. PMID: 34872869; PMCID: PMC8721059.
14. Almeida Silva HJ, Barbosa GM, Scatone Silva R, Saragiotto BT, Oliveira JMP, Pinheiro YT, Lins CAA, de Souza MC. Dry cupping therapy is not superior to sham cupping to improve clinical outcomes in people with non-specific chronic low back pain: a randomised trial. *J Physiother*, 2021; 67(2): 132-139. doi: 10.1016/j.jphys.2021.02.013. Epub 2021 Mar 20. PMID: 33757719.
15. Maniaci A, Merlino F, Cocuzza S, Iannella G, Vicini C, Cammaroto G, Lechien JR, Calvo-Henriquez C,

- La Mantia I. Endoscopic surgical treatment for rhinogenic contact point headache: systematic review and meta-analysis. *Eur Arch Otorhinolaryngol*, 2021; 278(6): 1743-1753. doi: 10.1007/s00405-021-06724-6. Epub 2021 Mar 6. Erratum in: *Eur Arch Otorhinolaryngol*, 2021; 278(11): 4615. doi: 10.1007/s00405-021-06844-z. PMID: 33677741; PMCID: PMC7936872.
16. Johnson MI, Paley CA, Jones G, Mulvey MR, Wittkopf PG. Efficacy and safety of transcutaneous electrical nerve stimulation (TENS) for acute and chronic pain in adults: a systematic review and meta-analysis of 381 studies (the meta-TENS study). *BMJ Open*, 2022; 10, 12(2): e051073. doi: 10.1136/bmjopen-2021-051073. PMID: 35144946; PMCID: PMC8845179.
17. Rogers AH, Farris SG. A meta-analysis of the associations of elements of the fear-avoidance model of chronic pain with negative affect, depression, anxiety, pain-related disability and pain intensity. *Eur J Pain*, 2022; 26(8): 1611-1635. doi: 10.1002/ejp.1994. Epub 2022 Jul 7. PMID: 35727200; PMCID: PMC9541898.
18. Turner AP, Jensen MP, Day MA, Williams RM. Behavioral activation and behavioral inhibition: An examination of function in chronic pain. *Rehabil Psychol*, 2021; 66(1): 57-64. doi: 10.1037/rep0000316. Epub 2020 Mar 9. PMID: 32150432; PMCID: PMC7483151.
19. Dubois B, López-Arrieta J, Lipschitz S, Doskas T, Spiru L, Moroz S, Venger O, Vermersch P, Moussy A, Mansfield CD, Hermine O, Tsolaki M; AB09004 Study Group Investigators. Masitinib for mild-to-moderate Alzheimer's disease: results from a randomized, placebo-controlled, phase 3, clinical trial. *Alzheimers Res Ther*, 2023; 28, 15(1): 39. doi: 10.1186/s13195-023-01169-x. Erratum in: *Alzheimers Res Ther*, 2023; 22, 15(1): 85. doi: 10.1186/s13195-023-01230-9. PMID: 36849969; PMCID: PMC9972756.
20. Turci AM, Nogueira CG, Nogueira Carrer HC, Chaves TC. Self-administered stretching exercises are as effective as motor control exercises for people with chronic non-specific low back pain: a randomised trial. *J Physiother*, 2023; 69(2): 93-99. doi: 10.1016/j.jphys.2023.02.016. Epub 2023 Mar 21. PMID: 36958977.
21. Yu Z, Yin Y, Wang J, Zhang X, Cai H, Peng F. Efficacy of Pilates on Pain, Functional Disorders and Quality of Life in Patients with Chronic Low Back Pain: A Systematic Review and Meta-Analysis. *Int J Environ Res Public Health*, 2023; 6, 20(4): 2850. doi: 10.3390/ijerph20042850. PMID: 36833545; PMCID: PMC9956295.
22. Mohamed SHP, Alatawi SF. Effectiveness of Kinesio taping and conventional physical therapy in the management of knee osteoarthritis: a randomized clinical trial. *Ir J Med Sci*, 2023; 192(5): 2223-2233. doi: 10.1007/s11845-022-03247-9. Epub 2022 Dec 17. PMID: 36527538; PMCID: PMC10522526.
23. Er G, Yüksel İ. A comparison of the effects of connective tissue massage and classical massage on chronic mechanical low back pain. *Medicine (Baltimore)*, 2023; 14, 102(15): e33516. doi: 10.1097/MD.00000000000033516. PMID: 37058058; PMCID: PMC10101266.
24. Honig LS, Sabbagh MN, van Dyck CH, Sperling RA, Hersch S, Matta A, Giorgi L, Gee M, Kanekiyo M, Li D, Purcell D, Dhadda S, Irizarry M, Kramer L. Updated safety results from phase 3 lecanemab study in early Alzheimer's disease. *Alzheimers Res Ther*, 2024; 10, 16(1): 105. doi: 10.1186/s13195-024-01441-8. Erratum in: *Alzheimers Res Ther*, 2024; 10, 16(1): 159. doi: 10.1186/s13195-024-01507-7. PMID: 38730496; PMCID: PMC11084061.
25. Sahara N, Higuchi M. Diagnostic and therapeutic targeting of pathological tau proteins in neurodegenerative disorders. *FEBS Open Bio*, 2024; 14(2): 165-180. doi: 10.1002/2211-5463.13711. Epub 2023 Sep 30. PMID: 37746832; PMCID: PMC10839408.
26. Salvesen L, Capriglia E, Dresler M, Bernardi G. Influencing dreams through sensory stimulation: A systematic review. *Sleep Med Rev*, 2024; 74: 101908. doi: 10.1016/j.smrv.2024.101908. Epub 2024 Feb 15. PMID: 38417380; PMCID: PMC11009489.
27. Paramento M, Passarotto E, Maccarone MC, Agostini M, Contessa P, Rubega M, Formaggio E, Masiero S. Neurophysiological, balance and motion evidence in adolescent idiopathic scoliosis: A systematic review. *PLoS One*, 2024; 22, 19(5): e0303086. doi: 10.1371/journal.pone.0303086. PMID: 38776317; PMCID: PMC11111046.
28. Wang J, Wu B, Tong Y, Wang X, Lu Z, Wang W. Effect of acupuncture combined with rehabilitation training on sensory impairment of patients with stroke: a network meta-analysis. *BMC Complement Med Ther*, 2024; 26, 24(1): 102. doi: 10.1186/s12906-024-04401-9. PMID: 38409065; PMCID: PMC10898000.
29. Ni Y, Li S, Lv X, Wang Y, Xu L, Xi Y, Sun Y, Bao J, Liao S, Li Y. Efficacy of sensory-based static balance training on the balance ability, aging attitude, and perceived stress of older adults in the community: a randomized controlled trial. *BMC Geriatr*, 2024; 11, 24(1): 49. doi: 10.1186/s12877-023-04596-5. PMID: 38212725; PMCID: PMC10782606.