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The Role of Sensorimotor Simulation in Emotion Recognition: Insights from a Meta-Analysis on individuals with Moebius Syndrome

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Chapter 1

Introduction

Emotions are functional, biological and cognitive responses to relevant stimuli that organize the mind (e.g. attention, perception, cognition, motivation) and the body (e.g. hormones, autonomic nervous system, sensory organs, muscle movements) in order to produce appropriate behavioral responses (Panksepp, 2005). In the words of Wood et al. (2016), “simply put, if brains evolved to move an organism through space, then emotions evolved to organize and direct that movement into an adaptive response”. Emotions are a combination of expressive, behavioral, physiological and subjective feeling responses; the activation of one component will consequently activate the others.

For a long time, affective neuroscientists sought to pinpoint specific regions of the brain associated with distinct emotions, aiming to understand the precise neural localization for each emotion. A new perspective, offered by the **embodied cognition** theoretical framework, has led to the question of whether cognition and emotion are not localized only in the brain but actually engage the whole body. According to this new perspective, states of the body modify states of the mind and vice versa. The mind is not the only resource at our disposal for solving problems: cognition embraces the brain, the body and the environment, creating an extended system assembled from diverse resources. Much of the effort required to accomplish our goals is performed by our body and its movements in the environment, directed by perception, which eliminates the need for intricate internal mental representations (Wilson & Golonka, 2013).

For example, although tactile sense is the primary function of the somatosensory cortex, somatosensory representations might contribute to the detection of emotions by connecting non-tactile perceptual signals to the physical states that correspond to every emotional state (Damasio, 1996). The right somatosensory cortex appears to be involved in the classification of emotions conveyed in other's vocal and facial expressions (Kragel & LaBar, 2016). Moreover, there is a correlation between the subjective experience generated by the subject's own expressions and the ability of this region to predict the emotions perceived in others. **Sensorimotor simulation**, a theory that falls under the umbrella of the aforementioned embodied cognition, might provide an insight on why that happens. The theory states that, in order to recognize other people's emotions, we imperceptibly replicate their facial expressions; the mechanism of facial feedback would then allow us to perceive that same emotion (Bogart & Matsumoto, 2010). This thesis project aims to analyze, through a meta-analysis, the perception of facial expressions in people with **Moebius syndrome** (MBS), a congenital facial paralysis. Since MBS individuals are unable from birth to produce facial expressions, they cannot exploit the sensorimotor simulation mechanism, thus proving to be the perfect population to study this phenomenon. According to what the model predicts, people with MBS should perform worse than controls in recognizing facial expressions. However, as we will see later, the findings of the studies in literature are rather discordant.

Chapter 2

Recognizing facial expressions

2.1 An overview of the models on emotion recognition

Emotion recognition is the process through which an individual converts meaningful explicit or implicit information about another's underlying emotional, motivational, and/or intentional state from their perception of the other's facial expression (or other nonverbal signal) to that signal (Wood, Rychlowska, et al., 2016).

2.1.1 Understanding face recognition

In 1986, Bruce and Young proposed a cognitive model for face processing according to which seven distinct types of information (pictorial, structural, visually derived semantic, identity-specific semantic, name, expression and facial speech codes) would be derived when we perceive a face; emotion recognition is one of them and would occur separately from facial recognition.

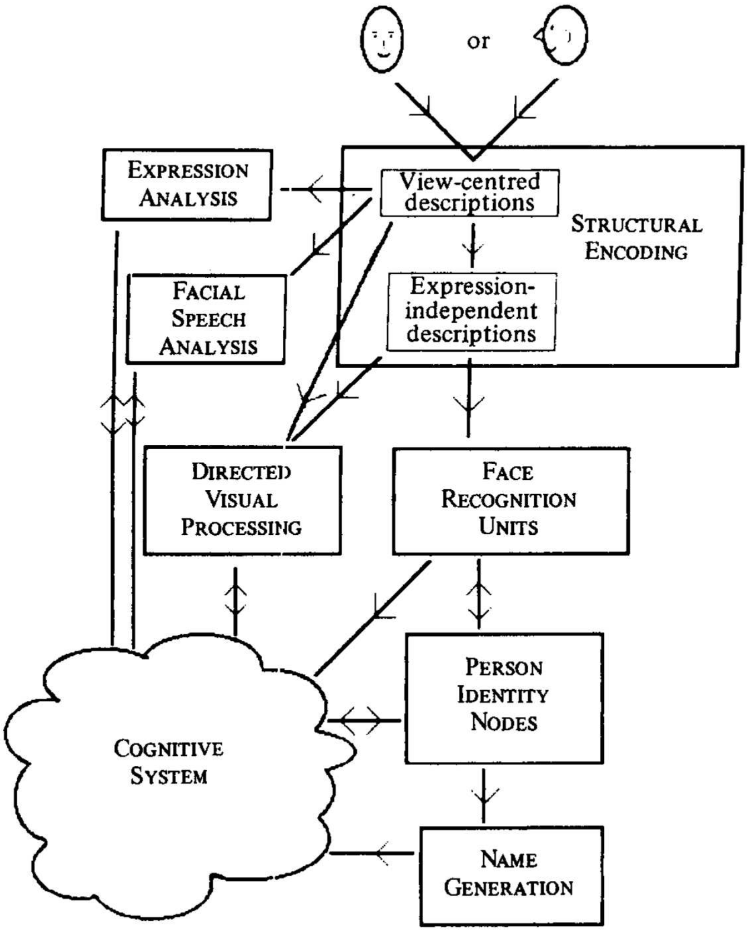


Figure 2.1: The diagram of the model of face recognition from the original article by Bruce & Young (1986)

The model (Figure 2.1) involves a series of sequential processing states organized hierarchically:

1. Structural encoding: generates a series of descriptions of the face that is seen, including more abstract and view-centered descriptions of the features and

the overall configuration.

2. Facial speech analysis: occurs through the categorization of the visible movements of the mouth and tongue.
3. Expression analysis: expression is categorized as a result of how different characteristics are configured.
4. Face recognition units (FRU): each FRU has stored structural codes that describe a known face. When a face is observed, the FRU will send a recognition signal to the cognitive system with an intensity that depends on the degree of similarity between the stored codes and the structural coding input. This level of activation can also be modulated indirectly through the person identity node, which is activated when we expect to see a specific person or because the face has been seen recently.
5. Person identity nodes (PIN): a portion of the associative memory where there are stored identity-specific semantic codes (according to the original model, we have one PIN per every person we know); PINs allow us to feel that we achieved the recognition of that specific person.
6. Name generation: accessed only *via* the person identity nodes.
7. Cognitive system: it contains or accesses all the associative and episodic data beyond the purview of our “person identity nodes”.

2.1.2 Distributed Neural System for Face Perception

Haxby and Gobbini (2011) proposed a model of face perception involving several brain areas (Figure 2.2) that cooperate in diverse arrangements to derive distinct sorts of information from faces (Haxby & Gobbini, 2011). The model (Figure 2.3) categorizes the brain regions involved in face perception into two systems: the Core System, occipitotemporal visual extrastriate areas that are crucial for visual analysis of faces, and the Extended System, neural systems whose functions are not predominantly visual but have important roles in deriving information from faces.

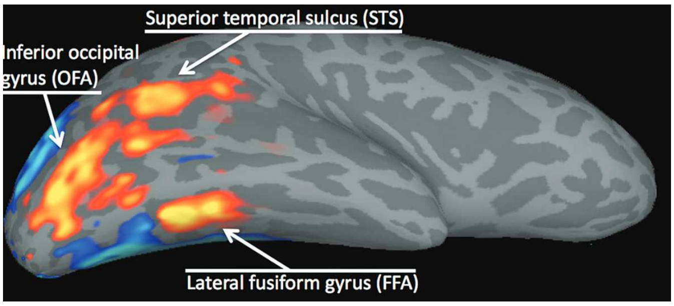


Figure 2.2: Extra-striate visual areas that are activated by the presentation of faces. Specifically, areas that respond more to images of faces than to images of houses or single objects. In the image, the cortical surface is inflated and flipped so that the cortex of the sulcus and the lateral and ventral surfaces are highlighted. Adapted from Haxby et al. (2000).

The same dissociation between static features (face and identity recognition) and dynamic features (speech and expression analysis) seen in Bruce and Young (1986), is maintained in the Core System, also on the anatomical level in the face-responsive cortices: the inferior occipital gyrus, also called **occipital face area** (OFA), and the fusiform gyrus, best known as **fusiform face area** (FFA), for recognizing facial identity, the **posterior superior temporal sulcus** (pSTS) for representation of changeable features, essential for facial gestures like expressions and eye gaze. In fact, several studies suggest that the STS is selectively activated by dynamic stimuli such as changing expression or gaze, while the FFA responds more intensively at variations of identity rather than gaze (Puce et al., 1998;

Hoffman & Haxby, 2000; Engell et al., 2006).

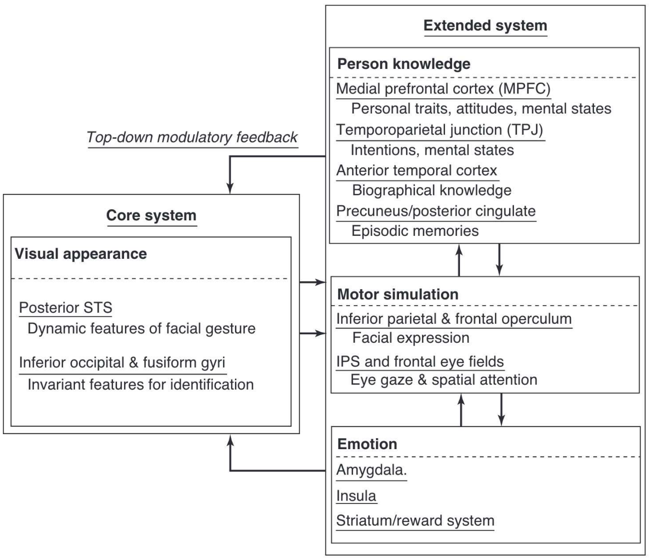


Figure 2.3: Updated model of distributed neural systems for face perception by Haxby & Gobbini (2011)

Regarding the Extended System, three sets of brain areas are implicated in the representation of person knowledge, action understanding (including gaze and attention), and emotion. The extrastriate cortex in the pSTS plays a major role in the visual processing of facial expression; however, in order to derive the meaning of the expression, we use a variety of brain regions that are active in action understanding and emotion. These regions are part of the Extended System.

The hypothesized human mirror neuron system (hMNS) is involved in facial expression perception, specifically the frontal operculum. This area is considered to reflect the role of motor representations of facial expressions necessary for understanding the meaning of others' expressions (Figure 2.4) (Carr et al., 2004; Montgomery and Haxby, 2008; Montgomery et al., 2009).

Mirror neurons, firstly discovered in single-unit recording studies in monkeys, become active when performing specific actions and observing other people executing the same actions (Di Pellegrino et al., 1992; Gallese et al., 1996; Rizzolatti et al., 2001; Grafton, 2009). In humans, where mirror neurons activation is measured through fMRI, the regions that show this behavior are the frontal operculum, premotor cortex and inferior parietal lobe (Haxby & Gobbini, 2011).

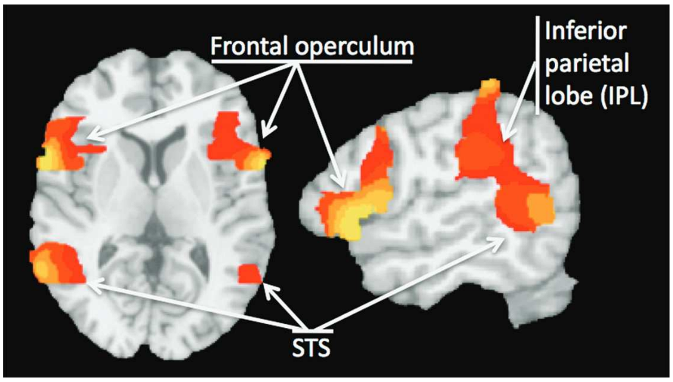


Figure 2.4: Brain areas active in vision, imitation, and production of facial expressions (Montgomery et al., 2009)

Additionally, the perception of expression stimulates activity in the emotional regions of the brain. For example, the amygdala, a region strongly connected with fear responses, is triggered by many facial expressions but responds most strongly to fear (Breiter et al., 1996; Morris et al., 1996; Whalen, 1998; Whalen et al., 1998, 2004).

This leads us to hypothesize that, in order to understand the emotional meaning of expressions, it is important to evoke the emotion itself; just as the hMNS would simulate the actions of others, similarly we would also mirror their emotions (Haxby & Gobbini, 2011). This activation would not induce a strong emotional experience, it would only contribute to the understanding of the observed expression.

Thus, different processes and areas would be involved in emotion recognition: the recognition of dynamic features carried by the pSTS, the motor simulation of facial expressions occurring in inferior parietal and frontal operculum, and activation of areas related to emotion processing for emotional understanding (e.g. amygdala, insula, striatum/reward system). Motor simulation plays a key role in the model proposed by Wood and colleagues (2016), which I will discuss in a following paragraph of this chapter. However, it is first necessary to mention the revision of of Haxby and Gobbini's model by Duchaine and Yovel (2015), in order to have a clear understanding of the current state of knowledge on face and expression recognition from a neural perspective.

2.1.3 A Revised Neural Framework for Face Processing

Duchaine and Yovel (2015) proposed a revision of the previous model based on more recent evidence, which appears to suggest the presence of additional face-sensitive areas. These areas would constitute two distinct and interconnected neural pathways: a ventral pathway for the representation of invariant aspects of the face and identity, and a dorsal pathway for processing dynamic aspects such as facial expressions and gaze.

The face-selective areas more recently discovered include the **anterior temporal lobe** (ATL-FA) (Rajimehr et al., 2009; Tsao et al., 2008), the **superior anterior temporal sulcus** (aSTS-FA) (Pitcher et al., 2011), and the **inferior frontal gyrus** (IFG-FA) (Figure 2.5) (Fox et al., 2009; Chan & Downing, 2011; Axelrod & Yovel, 2013).

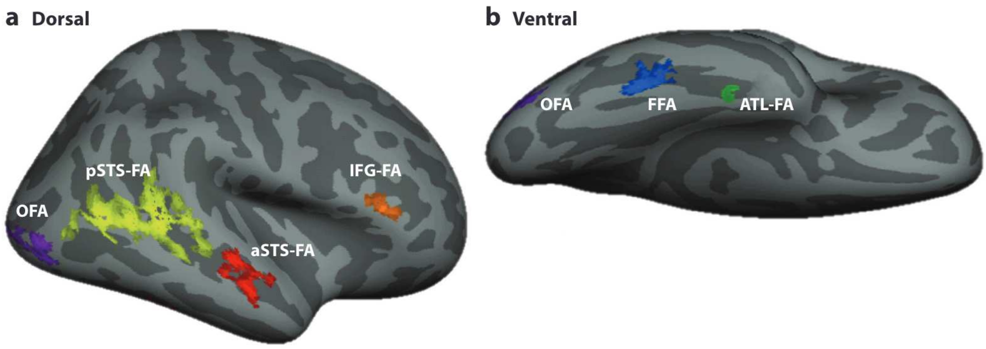


Figure 2.5: Regions Specialized for Face Processing. (a) Dorsal face-processing regions: posterior superior temporal sulcus face area (pSTS-FA), anterior superior temporal sulcus face area (aSTS-FA), and inferior frontal gyrus face area (IFG-FA). (b) Ventral face-processing regions: occipital face area (OFA), fusiform face area (FFA), and anterior temporal lobe face area (ATL-FA) (Duchaine & Yovel, 2015).

According to Duchaine and Yovel, these areas, along with OFA, FFA, and pSTS, would give rise to two distinct neural streams (Figure 2.6):

- **Ventral Stream**: OFA, FFA, and ATL-FA; the areas in the ventral stream preferentially encode information about facial shape, serving as the primary mechanism for the representation of invariant features such as identity, gender, and age, and contributing to facial expression detection.
  - OFA: This area appears to be specialized in representing face parts (Pitcher et al., 2007); in fact, it is not responsive to faces with poorly defined facial parts, such as Mooney faces (Rossion et al., 2011). This area is closely connected to the FFA and ATL-FA, but the nature of its connections with dorsal stream structures remains unclear (Gschwind et al., 2012; Pitcher et al., 2014; Pyles et al., 2013).
  - FFA: it processes information related to facial identity (Gilaie-Dotan

  & Malach, 2007; Grill-Spector et al., 2004; Hoffman & Haxby, 2000; Rotshtein et al., 2005; Winston et al., 2003; Yovel & Kanwisher, 2005) and also contributes to the perception of facial expressions, considering its general function in representing form information (Dalrymple et al., 2011; Fox et al., 2009; Furl et al., 2007; Ganel et al., 2005; Ishai et al., 2004; Kadosh et al., 2010; Vuilleumier et al., 2001; Xu & Biederman, 2010).

  - ATL-FA: The function of this region is not entirely clear, but it may store consistent information about facial identity (Anzellotti et al., 2013; Yang et al., 2015; Collins & Olson, 2014). This hypotesis is in line with a similar area found in macaques, called AM, which encodes identity regardless of expression (Freiwald & Tsao, 2010).

- **Dorsal Stream**: pSTS-FA, aSTS-FA, and IFG-FA; these areas likely represent dynamic aspects of the face, such as expression, gaze, and mouth movements since they exhibit higher activation in response to dynamic rather than static faces.

  - pSTS-FA: receives information about motion and shape from early visual areas (Dalrymple et al., 2011; Steeves et al., 2006). Connectivity research has revealed strong links between STS and IFG, consistent with previous studies of brain connections. Nevertheless, further studies are required to gain a deeper understanding of these connections and the specific roles of the areas involved in face perception. Furthermore, it has been observed that the STS area responds to both moving faces and human voices, suggesting a potential role in multimodal face processing.

- aSTS-FA: it might process the orientation of eye gaze (Calder et al., 2007; Carlin et al., 2011)
- IFG-FA: it is possibly associated with eye movements and the encoding of gaze information, due to the proximity to the frontal eye fields (Chan Downing, 2011).

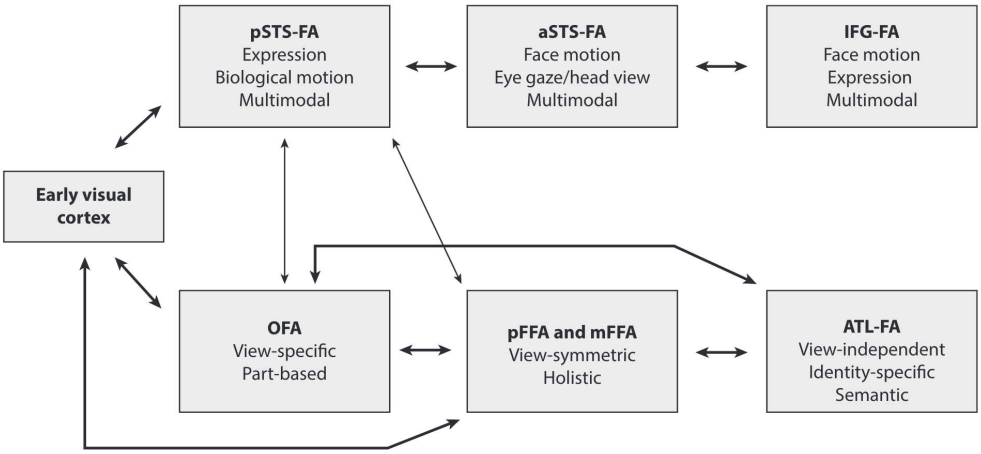


Figure 2.6: Updated model illustrating the functions and interactions of face-selective regions (Duchaine & Yovel, 2015).

2.2 The sensorimotor simulation

The sensorimotor simulation offers insights into the potential mechanisms underlying facial expression recognition, providing clarity on the involvement of both frontal and dorsal areas. The idea posits that when we recognize facial expressions, we internally mirror or simulate the observed expression. This neural mimicry might then evoke the associated emotion within the observer (Bogart Matsumoto, 2010).

The **sensorimotor simulation**, as defined by Wood and colleagues (2016) is a set of processes that features the subthreshold reproduction of the motor and somatosensory neural processes involved in the production of a facial expression. Using the words of the authors "Looking at another person's facial expression of emotion can trigger the same neural processes involved in producing the expression, and such responses play a functional role in emotion recognition". The simulation, which occurs while we observe the other person's face, triggers the activation of the emotional state associated with it, allowing the observer to infer the feeling that the person is expressing more accurately and quickly.

The automatic and unconscious facial muscle activity that can be present in sensorimotor simulation is called **facial mimicry**, a low-level, spontaneous, motor response that frequently occurs in the perceiver of a facial expression (Wood, Rychlowska, et al., 2016). It is important to emphasize that mimicry is not mandatory, since simulation can also occur on the basis of neural activation alone. Notably, copying facial expressions is a universal trait of social interactions and is present in other primate species (Figure 2.7) (Mancini et al., 2013; Palagi et al., 2019).

Figure 2.7: An example of rapid facial mimicry in primates. Photo by P.F. Ferrari, from Mancini et al. (2013)

When a person observes a happy expression, for instance, it is possible to measure an increased electromyographic (EMG) activity of zygomaticus major muscle, which is responsible for smiling; when perceiving an angry expression, there might be an increase in the EMG activity of the corrugator supercilii, the muscle responsible for frowning (De Stefani et al., 2019). Normally, the perceiver flexes the same facial muscles implicated in the observed facial expression, but prior information or expectations might affect the expression they "mimic" (Halberstadt & Niedenthal, 2001).

The model goes further, arguing that, in order to accurately recognize the expression, the simulation would actually activate - fully or partially - the associated emotion in the perceiver's brain, all to accurately recognize the expression. This is directly connected to the facial feedback hypothesis, which claims that proprioceptive input from facial expressions is either essential or sufficient to impact the perception of emotion (Izard, 1971; Tomkins 1962, 1963).

2.2.1 An outline of the model

In order to understand the model more clearly, we can use as a reference the diagram reported in the original article by Wood et al. (2016) (Figure 2.8).

When the perceiver observes the expression of fear on the expresser (A), the face region of the motor cortex is activated, together with other motor control areas (B). Facial mimicry might be present at this stage. (C) The activity of the premotor, motor and somatosensory cortices produces activation in brain regions implicated in fear states (Price & Harmon-Jones, 2015), which is followed by psychological, cognitive and behavioral changes (D) or simulation of those states. (E) When the

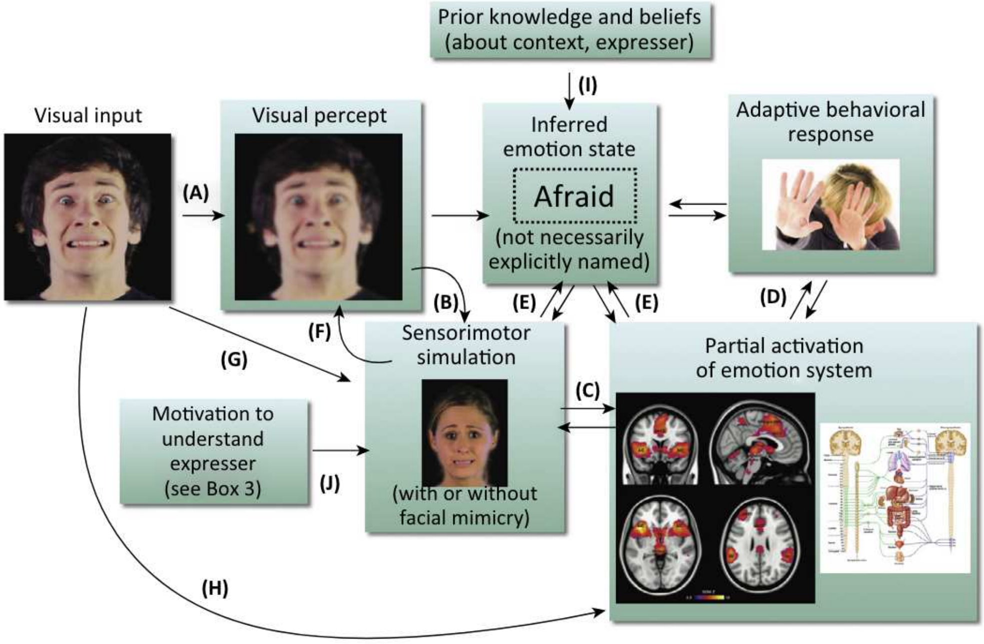


Figure 2.8: An outline of the model by Wood et al., 2016

fear state is partially activated, the perceiver can either explicitly or implicitly identify the expresser's emotion. (F) It appears that the sensorimotor simulation iteratively modifies the visual percept's clarity (Wood et al., 2016). Conscious awareness is not a requirement for (G) simulation and (H) emotional responding (Tamietto et al., 2009). (I) Conceptual understanding of emotions plays a role in the inferred emotion state (Hess & Hareli, 2015), whereas affiliation with and motivation to comprehend the expresser (J) influence the chance that sensorimotor simulation and facial mimicry will take place. While box-and-arrow diagrams like the one shown in the image tend to imply neural modularity and a specific sequence of events, the authors are keen to highlight the distributed and recursive nature of the emotion perception process, which repeatedly recruits the visual, somatosensory, motor, and premotor cortices as well as, at the subcortical level, portions of the limbic system and brainstem (Wood et al., 2016).

2.2.2 Evidence supporting the sensorimotor simulation

The presence of a simulation process underlying the recognition of facial expressions is supported by at least three lines of research, specifically: 1) evidence from studies with blocked facial mimicry, 2) evidence from neuroimaging studies, and 3) evidence from patients with brain lesions and subjects with simulated lesions (Sessa et al., 2022).

2.2.2.1 Blocking facial mimicry

A series of studies where mimicry was blocked through different techniques (you can see an example in Figure 2.9, bottom panel), showed an association between imitation blocking and recognition of emotional expressions. In a study conducted by Wood, Lupyan et al. (2016), participants whose facial mimicry was blocked through the use of a gel facemask showed a poorer ability to distinguish target expressions from very similar distractors when compared to participants who could freely use their facial mimicry. When mimicry in the lower part of the face is obstructed, the recognition of happy facial and body expressions is hindered (Figure 2.9, top panel) (Borgomaneri et al., 2020). In addition, blocking facial imitation also reduces the ability to distinguish between real and fake smiles, to the extent that they were judged equally genuine (Rychlowska et al., 2014).

2.2.2.2 Evidence from neuroimaging studies

According to different neuroimaging studies, the premotor, somatosensory, and gustatory cortices are among the brain areas implicated in the creation and

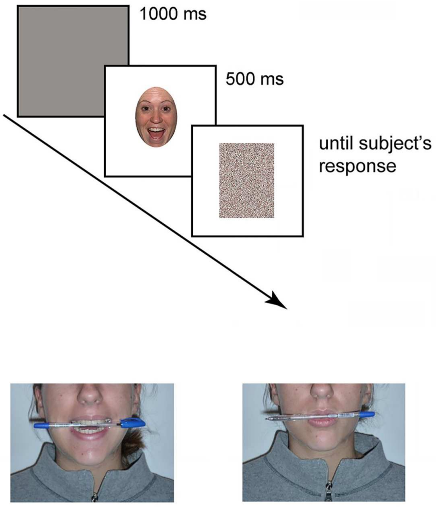


Figure 2.9: An example of face manipulation used to alter facial mimicry (Borgomaneri et al., 2020)

detection of emotional responses. Kircher and colleagues (2013), found that the pre-supplementary motor area is a core-shared representation-structure that reinforce the observation and execution of affective contagious facial expressions: it may even play a modulatory role in the preparation of performing happy facial expressions. In another study, researchers found that observing disgusted faces and smelling disgusting odors activates the same areas in the anterior insula and anterior cingulate cortex, although to a lesser extent for the latter (Figure 2.10) (Wicker et al., 2003).

2.2.2.3 Evidence from patients with lesions and virtual lesions

Studies on patients with crucial brain lesions, as well as healthy people who underwent transcranial magnetic stimulation (TMS) in order to simulate lesions, have produced a convincing body of data that supports the model. In particular,

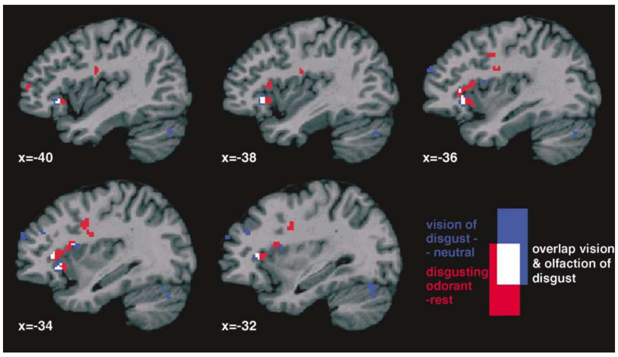


Figure 2.10: Illustration of the overlap (in white) between brain activation during observation (in blue) and sensation (in red) of disgust (Wicker et al., 2003)

a study on subjects with focal brain lesions showed that somatosensory-related cortices might be fundamental to perform emotion recognition of facial expressions (Adolphs et al., 2000). The use of TMS on the somatosensory cortices interfered with a fast matching task in which participants were asked if the second emotional face was the same as the first (Pourtois et al., 2004).

2.2.3 Evidence against the sensorimotor simulation

Although the studies just examined appear to support the sensorimotor simulation hypothesis, other lines of research, on the contrary, suggest that simulation is not present or, at least, is not a fundamental component of emotion recognition. One particular clinical condition seems to highlight this discordance: Moebius syndrome (MBS) (Figure 2.11), a congenital condition characterized by “nonprogressive uni- or bi-lateral facial (i. e. VII cranial nerve) and abducens (i. e. VI cranial nerve) palsy” (Picciolini et al., 2016). The facial paralysis implicates the inability to engage facial muscles and produce expressions, therefore, according to the sensorimotor simulation model, the capability of reactivating expression-specific sensory representations and facial mimicry should be constrained in some way, even if the paralysis is partial (Sessa et al., 2022). If the performance of these patients in emotion recognition does result to be normotypical, according to critics of the theory, this should be a compelling refutation of the simulation models.

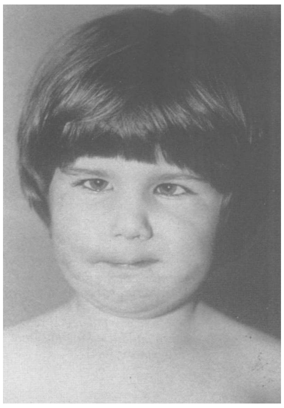


Figure 2.11: Three years old girl with Moebius syndrome (Kumar D., 1990).

At this moment, it is unclear whether the emotion recognition performance of individuals with the syndrome is evidence in favor or against sensorimotor simulation. As a matter of fact, the few studies focused on patients with MBS have used specific tests in which subjects were required to match a label to a facial expression, providing rather ambiguous results (De Stefani et al., 2019). While some authors found reliable impairments in emotion recognition (e.g. Belluardo et al., 2022), other studies showed normotypical performance in subjects with MBS, with no significant differences from the controls (e.g. Vannuscorps et al., 2020). This will be discussed in more details later. Overall, when present, emotion recognition deficits are often not severe and do not hinder people from leading full, rich emotional lives as adults (De Stefani et al., 2019).

Chapter 3

Moebius syndrome

Moebius syndrome (MBS) is a rare condition characterized by unilateral or bilateral nonprogressive congenital facial palsy (VII cranial nerve) with defects of ocular abduction (VI cranial nerve) (Figure 3.1); it may also be accompanied by additional cranial nerve (CN) palsies, orofacial deformities, and limb malformations (Broussard et al., 2008). This condition was reported for the first time in 1880 by the German ophthalmologist Von Graefe, albeit the name comes from the German neurologist and psychiatrist Paul Julius Möbius, who described signs and symptoms of the syndrome in more detail. According to estimates, MBS affects both sexes equally and occurs in 1/250.000 live births (Picciolini et al., 2016). The two main signs of the syndrome are: a mask-like facial expression or complete or partial facial paralysis (due to malformation of the 7th cranial nerve) (Calder et al., 2000) and missing lateral movement of the eyes (related to the 6th cranial nerve). This syndrome is often identified shortly after birth and is characterized by drooling, difficulty sucking, and inadequate eyelid closure during sleep; while the "mask-like facies" is notable later, when it becomes evident that the child does not move the face muscles neither when smiling nor when crying (Kumar D., 1990).

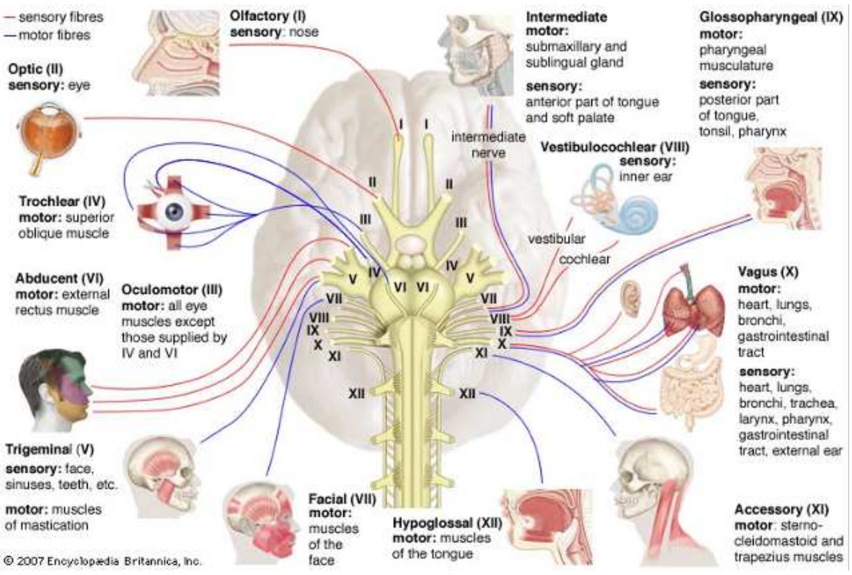


Figure 3.1: The cranial nerves (I-XII) and their areas of innervation (Encyclopædia Britannica, Inc.).

3.1 Criteria of diagnosis

Since this syndrome is rare, investigations of the frequencies of related traits is scarce and the multitude of MBS-related traits creates diagnostic ambiguity (Bell et al., 2019). As a result, making a diagnosis is challenging, and it is also hard to define rigid diagnostic standards. Indicatively, as a reference, it is possible to consider the criteria for diagnosis proposed by Kumar D. in 1990:

1. The diagnosis of MBS requires total or partial facial nerve paralysis;
2. There are often present limb malformations including syndactyly, brachy-

dactyly or missing digits, and talipes;

3. The presence of the following additional clinical signs in conjunction with whole or partial facial nerve (VII) paralysis might also be useful in establishing a clinical diagnosis of Moebius syndrome (Figure 3.2):
    (a) oculomotor (III) and trochlear (IV) nerve palsies, which can be bilateral or unilateral and often affect the abducens (VI) nerve (Figure 3.3);
    (b) tongue hypoplasia caused by paralysis of the hypoglossal (XII) nerve;
    (c) problems speaking and swallowing due to trigeminal (V), glossopharyngeal (IX), and vagus (X) nerve palsies;
    (d) orofacial defects including bifid uvula, micrognathia, and ear malformations;
    (e) other musculoskeletal anomalies such as the Klippel-Feil anomaly, rib defects, and brachial muscle defects; and the absence of the sternal head of the pectoralis major.

3.2 Studying Moebius syndrome to investigate the sensorimotor simulation

As previously mentioned, Moebius syndrome is a congenital condition. Therefore, since their birth, people with MBS are not able to articulate emotions with their facial expressions. Thus, theoretically, people with MBS should not be able to use sensorimotor simulation as a mechanism to recognize facial expressions. If, as proponents of the model claim, such a mechanism plays an essential role in emotion

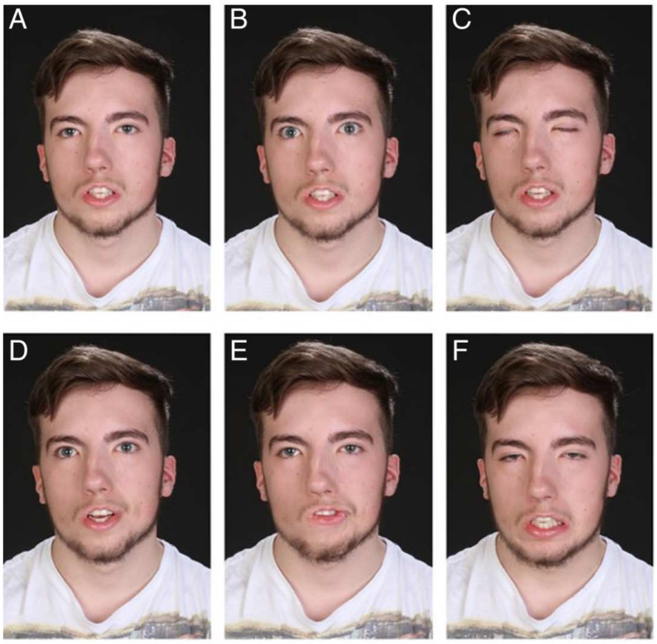


Figure 3.2: Classic Moebius facies of bilateral mixed facial palsy (McKay et al., 2016).

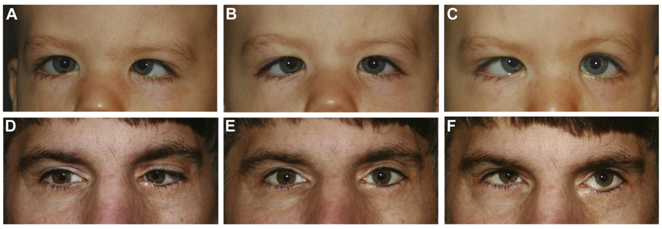


Figure 3.3: Eye alignment and horizontal ocular motility patterns in 2 patients with classic Moebius syndrome (MacKinnon et al., 2014).

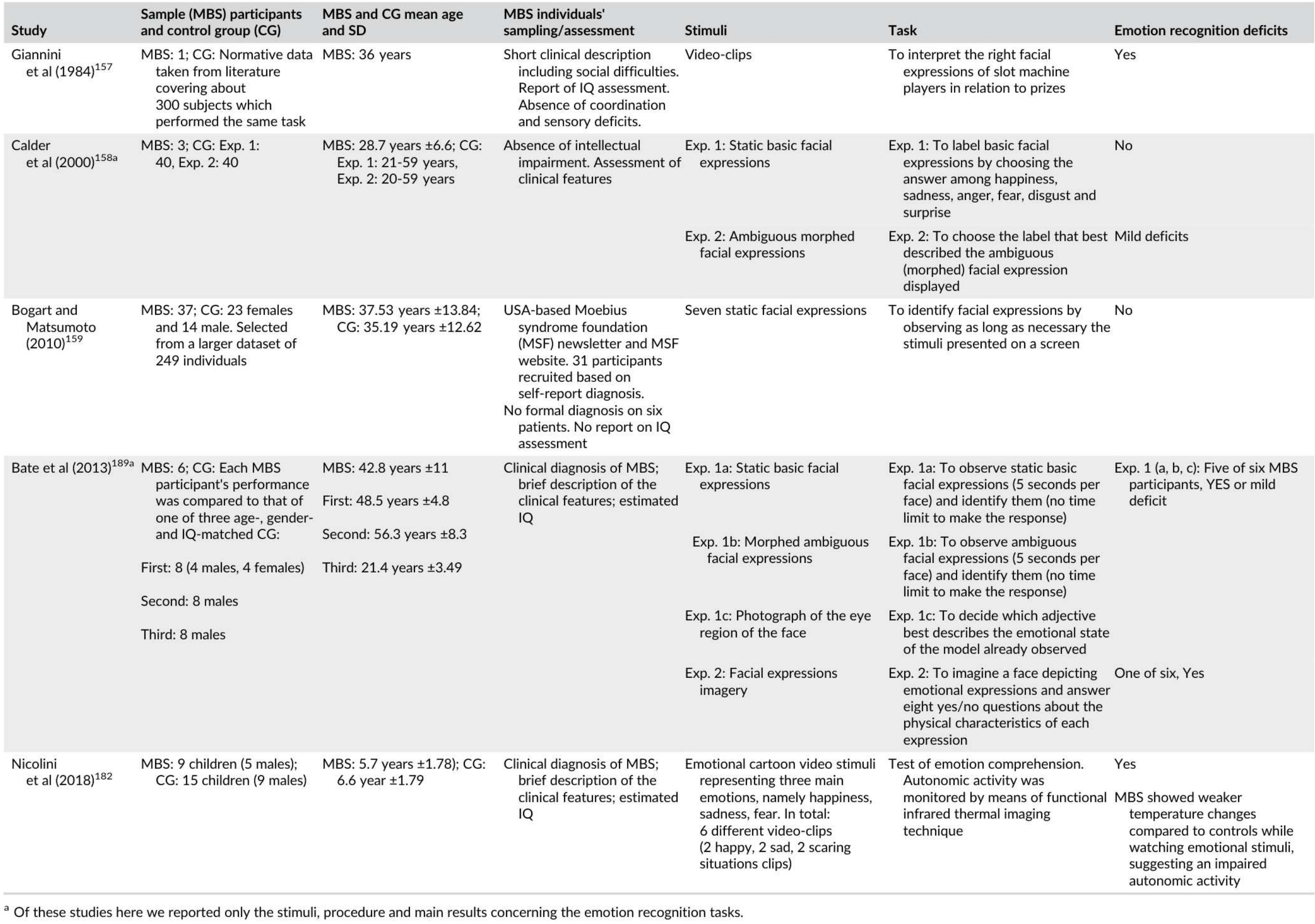
recognition, or at least a facilitating function, individuals with MBS should perform worse on these tasks. People with MBS thus turn out to be the ideal subjects to test the model. As we shall see in the next section, although the types of tasks proposed in different studies on the subject are similar, the results are notably divergent.

Chapter 4

Why a meta-analysis?

Considering the number of experimental studies already produced on the topic and the existence of only one review (De Stefani, 2019), we reckoned necessary to develop a compilation of works that would not only collect and summarize what has been done so far, but also provide an estimate of the effect.

Besides, a replicability problem has been found in this type of studies, as similar paradigms have produced rather different results, which in turn have led to equally different interpretations. A clear example of the incongruence in the results of the studies is emphasized by the table reported in the review conducted by De Stefani et al. (2019) (Figure 4.1). The table below summarizes the papers analyzed in the review. As it can be noted, the number of studies is not vast and the tasks used are quite diverse. This may have led to different results, with almost half of the papers finding deficits whilst the rest did not.



Study	Sample (MBS) participants and control group (CG)	MBS and CG mean age and SD	MBS individuals' sampling/assessment	Stimuli	Task	Emotion recognition deficits
Giannini et al (1984)[157]	MBS: 1; CG: Normative data taken from literature covering about 300 subjects which performed the same task	MBS: 36 years	Short clinical description including social difficulties. Report of IQ assessment. Absence of coordination and sensory deficits.	Video-clips	To interpret the right facial expressions of slot machine players in relation to prizes	Yes
Calder et al (2000)[158a]	MBS: 3; CG: Exp. 1: 40, Exp. 2: 40	MBS: 28.7 years ±6.6; CG: Exp. 1: 21-59 years, Exp. 2: 20-59 years	Absence of intellectual impairment. Assessment of clinical features	Exp. 1: Static basic facial expressions	Exp. 1: To label basic facial expressions by choosing the answer among happiness, sadness, anger, fear, disgust and surprise	No
				Exp. 2: Ambiguous morphed facial expressions	Exp. 2: To choose the label that best described the ambiguous (morphed) facial expression displayed	Mild deficits
Bogart and Matsumoto (2010)[159]	MBS: 37; CG: 23 females and 14 male. Selected from a larger dataset of 249 individuals	MBS: 37.53 years ±13.84; CG: 35.19 years ±12.62	USA-based Moebius syndrome foundation (MSF) newsletter and MSF website. 31 participants recruited based on self-report diagnosis. No formal diagnosis on six patients. No report on IQ assessment	Seven static facial expressions	To identify facial expressions by observing as long as necessary the stimuli presented on a screen	No
Bate et al (2013)[189a]	MBS: 6; CG: Each MBS participant's performance was compared to that of one of three age-, gender- and IQ-matched CG: First: 8 (4 males, 4 females) Second: 8 males Third: 8 males	MBS: 42.8 years ±11 First: 48.5 years ±4.8 Second: 56.3 years ±8.3 Third: 21.4 years ±3.49	Clinical diagnosis of MBS; brief description of the clinical features; estimated IQ	Exp. 1a: Static basic facial expressions	Exp. 1a: To observe static basic facial expressions (5 seconds per face) and identify them (no time limit to make the response)	Exp. 1 (a, b, c): Five of six MBS participants, YES or mild deficit
				Exp. 1b: Morphed ambiguous facial expressions	Exp. 1b: To observe ambiguous facial expressions (5 seconds per face) and identify them (no time limit to make the response)	
				Exp. 1c: Photograph of the eye region of the face	Exp. 1c: To decide which adjective best describes the emotional state of the model already observed	
				Exp. 2: Facial expressions imagery	Exp. 2: To imagine a face depicting emotional expressions and answer eight yes/no questions about the physical characteristics of each expression	One of six, Yes
Nicolini et al (2018)[182]	MBS: 9 children (5 males); CG: 15 children (9 males)	MBS: 5.7 years ±1.78); CG: 6.6 year ±1.79	Clinical diagnosis of MBS; brief description of the clinical features; estimated IQ	Emotional cartoon video stimuli representing three main emotions, namely happiness, sadness, fear. In total: 6 different video-clips (2 happy, 2 sad, 2 scaring situations clips)	Test of emotion comprehension. Autonomic activity was monitored by means of functional infrared thermal imaging technique	Yes MBS showed weaker temperature changes compared to controls while watching emotional stimuli, suggesting an impaired autonomic activity

[a] Of these studies here we reported only the stimuli, procedure and main results concerning the emotion recognition tasks.

Figure 4.1: Table reported by De Stefani et al. (2019) summarizing previous studies on emotion recognition in MBS.

Chapter 5

Methods

5.1 Focus of the meta-analysis

The objective of this study is to conduct a meta-analysis and derive effect size measures from the literature that examines emotion recognition abilities in individuals with Moebius syndrome. The premise is that a significant effect size would indicate a genuine impairment in individuals with MBS, bolstering the sensorimotor simulation theory. Conversely, if no difference in emotion recognition between individuals with MBS and control participants without paralysis is found, it would challenge the validity of this case as evidence for the theory. Instead, it would prompt us to explore why no differences exist, guiding us to fresh inquiries and a novel research trajectory.

The following meta-analysis was conducted according to the recent guidelines "The PRISMA 2020 Statement: an Updated Guideline for Reporting Systematic

Reviews” (Page et al., 2021).

5.2 Search strategy

Three different databases were searched: Web of Science, Scopus and Pubmed. The search was interrupted in April 2023. The strings used are the following:

Web of Science (the search was conducted in the section Topic “TS”):
(facial feedback hypothesis OR feedback OR motor simulation OR mimicry OR Embodied simulation theory OR Emotion recognition OR emotional processing OR mirror neuron system) AND (moebius) AND (fac*)

Scopus (the search was conducted in the sections “article title”, “abstract” and “keywords”):
(facial feedback hypothesis OR feedback OR motor simulation OR mimicry OR Embodied simulation theory OR Emotion recognition OR emotional processing OR mirror neuron system) AND (moebius) AND (fac*)

Pubmed (the search was conducted in the section “All fields”):
(facial feedback hypothesis OR feedback OR motor simulation OR mimicry OR Embodied simulation theory OR Emotion recognition OR emotional processing OR mirror neuron system) AND (moebius) AND (face OR facial)

The results obtained for the single keywords and their combinations can be found in Appendix A.

5.3 Eligibility criteria

The articles were selected according to a series of inclusion and exclusion criteria discussed beforehand. Studies were included if:

- already published or available online to avoid possible bias;
- included at least one subject with Moebius syndrome;
- contained a facial expression recognition task;
- written in English.

Studies were excluded if:

- did not report behavioral measures of facial expression recognition;
- concerned participants with paralysis that did not fit the diagnosis of MBS;
- investigated the medical aspects of the syndrome and not the psychological implications;
- were reviews, posters, meta-analyses, conference papers.

At first, a total of 51 papers were collected. After deduplication, 30 articles were left. A first screening of abstract and title excluded 19 papers that did not match the inclusion and exclusion criteria discussed in the previous paragraph. A following screening that took into account the full text of the articles excluded 4 more papers, leaving 7 relevant papers that matched all the criteria. The following flowchart (Figure 5.1) summarizes the selection process.

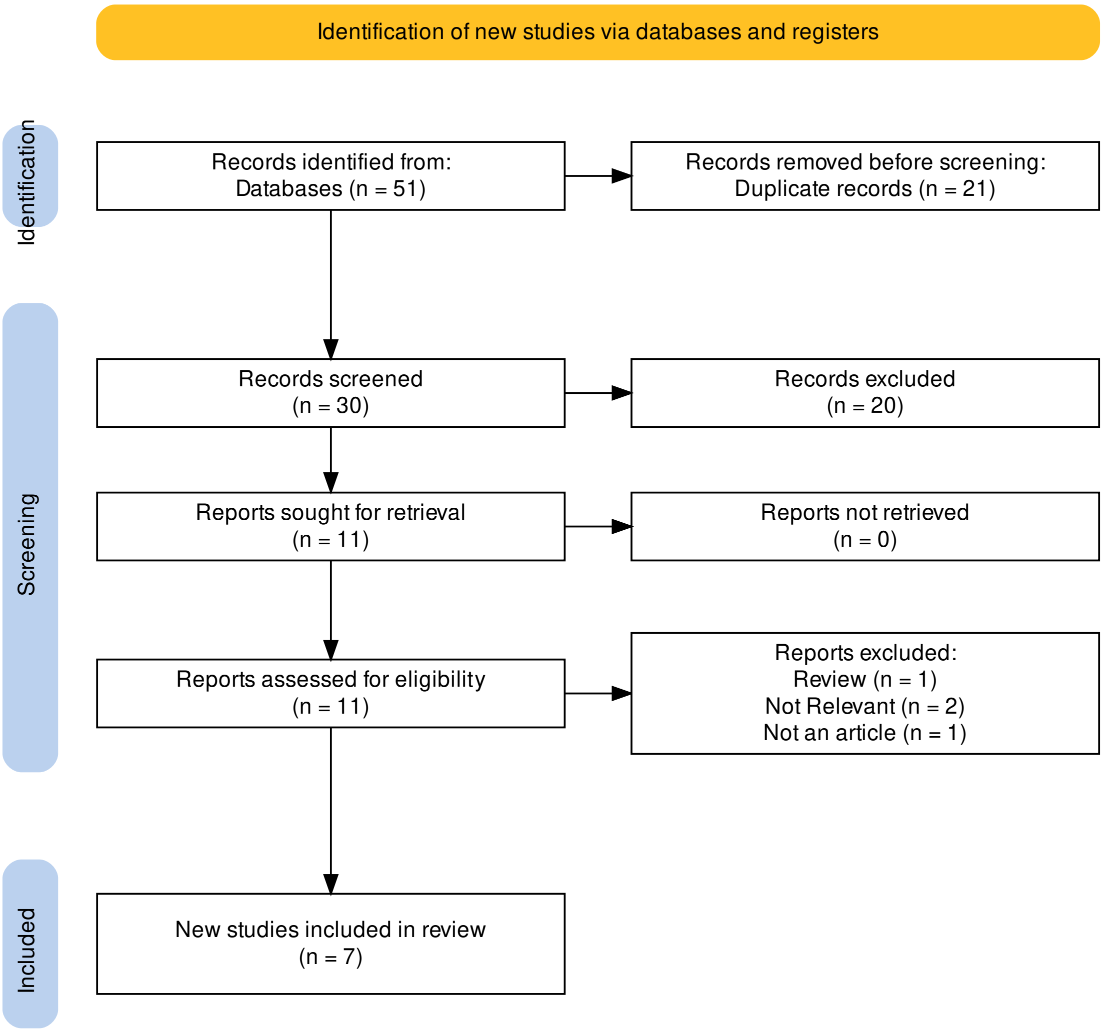


Figure 5.1: Flow diagram that indicates the number of records identified, included and excluded, and the reasons for exclusions. Created according to the PRISMA 2020 Statement (Page et al., 2021).

5.3.1 Studies collected

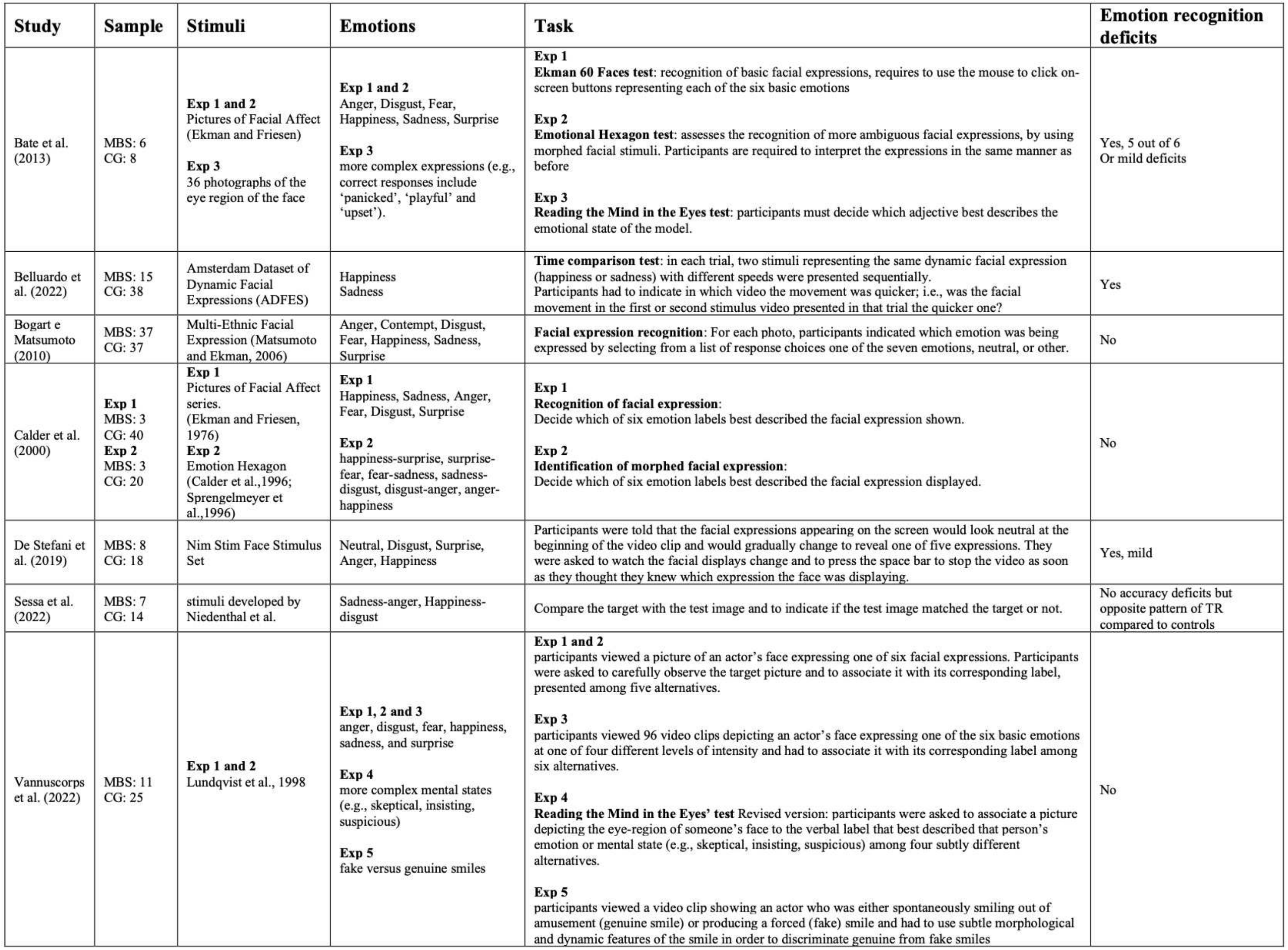
Here are the papers included in the final analysis:

- Bate, S., Cook, S. J., Mole, J., & Cole, J. (2013). **First Report of Generalized Face Processing Difficulties in Möbius Sequence**. PLoS ONE, 8(4). Scopus.
- Belluardo, M., De Stefani, E., Barbot, A., Bianchi, B., Zannoni, C., Ferrari, A., Rayson, H., Nuovo, S. D., Belluardo, G., Sessa, P., & Ferrari, P. F. (2022). **Facial Expression Time Processing in Typical Development and in Patients with Congenital Facial Palsy.** Brain Sciences, 12(5), 516.
- Bogart, K. R., & Matsumoto, D. (2010). **Facial mimicry is not necessary to recognize emotion: Facial expression recognition by people with Moebius syndrome.** Social Neuroscience, 5(2), 241–251.
- Calder, A. J., Keane, J., Cole, J., Campbell, R., & Young, A. W. (2000). **Facial expression recognition by people with mobius syndrome.** Cognitive Neuropsychology, 17(1–3), 73–87. Scopus.
- De Stefani, E., Ardizzi, M., Nicolini, Y., Belluardo, M., Barbot, A., Bertolini, C., Garofalo, G., Bianchi, B., Coude, G., Murray, L., & Ferrari, P. F. (2019). **Children withfacial paralysis due to Moebius syndrome exhibit reduced autonomic modulation during emotion processing.** Journal of Neurodevelopmental Disorders, 11, 12.
- Sessa, P., Schiano Lomoriello, A., Duma, G. M., Mento, G., De Stefani, E., & Ferrari, P. F. (2022). **Degenerate pathway for processing smile and other emotional expressions in congenital facial palsy: An hdEEG**

investigation. Philosophical Transactions of the Royal Society B-Biological Sciences, 377(1863), 20210190.

- Vannuscorps, G., Andres, M., & Caramazza, A. (2020). **Efficient recognition of facial expressions does not require motor simulation.** eLife, 9, 1–16. Scopus.

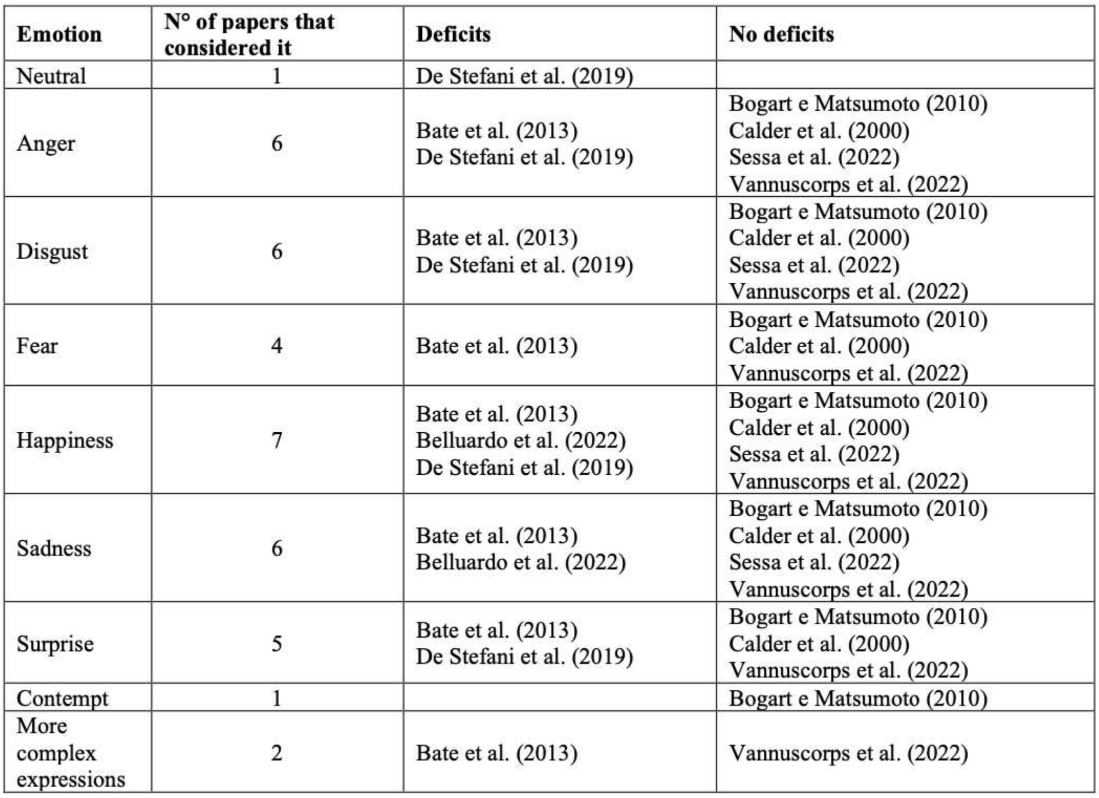
The following table (Figure 5.2) summarizes the studies in brief:



Study	Sample	Stimuli	Emotions	Task	Emotion recognition deficits
Bate et al. (2013)	MBS: 6 CG: 8	**Exp 1 and 2** Pictures of Facial Affect (Ekman and Friesen) **Exp 3** 36 photographs of the eye region of the face	**Exp 1 and 2** Anger, Disgust, Fear, Happiness, Sadness, Surprise **Exp 3** more complex expressions (e.g., correct responses include 'panicked', 'playful' and 'upset').	**Exp 1** **Ekman 60 Faces test**: recognition of basic facial expressions, requires to use the mouse to click on-screen buttons representing each of the six basic emotions **Exp 2** **Emotional Hexagon test**: assesses the recognition of more ambiguous facial expressions, by using morphed facial stimuli. Participants are required to interpret the expressions in the same manner as before **Exp 3** **Reading the Mind in the Eyes test**: participants must decide which adjective best describes the emotional state of the model.	Yes, 5 out of 6 Or mild deficits
Belluardo et al. (2022)	MBS: 15 CG: 38	Amsterdam Dataset of Dynamic Facial Expressions (ADFES)	Happiness Sadness	**Time comparison test**: in each trial, two stimuli representing the same dynamic facial expression (happiness or sadness) with different speeds were presented sequentially. Participants had to indicate in which video the movement was quicker; i.e., was the facial movement in the first or second stimulus video presented in that trial the quicker one?	Yes
Bogart e Matsumoto (2010)	MBS: 37 CG: 37	Multi-Ethnic Facial Expression (Matsumoto and Ekman, 2006)	Anger, Contempt, Disgust, Fear, Happiness, Sadness, Surprise	**Facial expression recognition**: For each photo, participants indicated which emotion was being expressed by selecting from a list of response choices one of the seven emotions, neutral, or other.	No
Calder et al. (2000)	**Exp 1** MBS: 3 CG: 40 **Exp 2** MBS: 3 CG: 20	**Exp 1** Pictures of Facial Affect series. (Ekman and Friesen, 1976) **Exp 2** Emotion Hexagon (Calder et al.,1996; Sprengelmeyer et al.,1996)	**Exp 1** Happiness, Sadness, Anger, Fear, Disgust, Surprise **Exp 2** happiness-surprise, surprise-fear, fear-sadness, sadness-disgust, disgust-anger, anger-happiness	**Exp 1** **Recognition of facial expression**: Decide which of six emotion labels best described the facial expression shown. **Exp 2** **Identification of morphed facial expression**: Decide which of six emotion labels best described the facial expression displayed.	No
De Stefani et al. (2019)	MBS: 8 CG: 18	Nim Stim Face Stimulus Set	Neutral, Disgust, Surprise, Anger, Happiness	Participants were told that the facial expressions appearing on the screen would look neutral at the beginning of the video clip and would gradually change to reveal one of five expressions. They were asked to watch the facial displays change and to press the space bar to stop the video as soon as they thought they knew which expression the face was displaying.	Yes, mild
Sessa et al. (2022)	MBS: 7 CG: 14	stimuli developed by Niedenthal et al.	Sadness-anger, Happiness-disgust	Compare the target with the test image and to indicate if the test image matched the target or not.	No accuracy deficits but opposite pattern of TR compared to controls
Vannuscorps et al. (2022)	MBS: 11 CG: 25	**Exp 1 and 2** Lundqvist et al., 1998	**Exp 1, 2 and 3** anger, disgust, fear, happiness, sadness, and surprise **Exp 4** more complex mental states (e.g., skeptical, insisting, suspicious) **Exp 5** fake versus genuine smiles	**Exp 1 and 2** participants viewed a picture of an actor's face expressing one of six facial expressions. Participants were asked to carefully observe the target picture and to associate it with its corresponding label, presented among five alternatives. **Exp 3** participants viewed 96 video clips depicting an actor's face expressing one of the six basic emotions at one of four different levels of intensity and had to associate it with its corresponding label among six alternatives. **Exp 4** **Reading the Mind in the Eyes' test** Revised version: participants were asked to associate a picture depicting the eye-region of someone's face to the verbal label that best described that person's emotion or mental state (e.g., skeptical, insisting, suspicious) among four subtly different alternatives. **Exp 5** participants viewed a video clip showing an actor who was either spontaneously smiling out of amusement (genuine smile) or producing a forced (fake) smile and had to use subtle morphological and dynamic features of the smile in order to discriminate genuine from fake smiles	No

Figure 5.2: Table 1: Summary of the relevant studies.

In the following table (Figure 5.3) the same studies have been reorganized according to the emotions taken into account, so as to return an overview of the deficits found -or not found- for each emotion:



Emotion	**N° of papers that considered it**	**Deficits**	**No deficits**
Neutral	1	De Stefani et al. (2019)	
Anger	6	Bate et al. (2013) De Stefani et al. (2019)	Bogart e Matsumoto (2010) Calder et al. (2000) Sessa et al. (2022) Vannuscorps et al. (2022)
Disgust	6	Bate et al. (2013) De Stefani et al. (2019)	Bogart e Matsumoto (2010) Calder et al. (2000) Sessa et al. (2022) Vannuscorps et al. (2022)
Fear	4	Bate et al. (2013)	Bogart e Matsumoto (2010) Calder et al. (2000) Vannuscorps et al. (2022)
Happiness	7	Bate et al. (2013) Belluardo et al. (2022) De Stefani et al. (2019)	Bogart e Matsumoto (2010) Calder et al. (2000) Sessa et al. (2022) Vannuscorps et al. (2022)
Sadness	6	Bate et al. (2013) Belluardo et al. (2022)	Bogart e Matsumoto (2010) Calder et al. (2000) Sessa et al. (2022) Vannuscorps et al. (2022)
Surprise	5	Bate et al. (2013) De Stefani et al. (2019)	Bogart e Matsumoto (2010) Calder et al. (2000) Vannuscorps et al. (2022)
Contempt	1		Bogart e Matsumoto (2010)
More complex expressions	2	Bate et al. (2013)	Vannuscorps et al. (2022)

Figure 5.3: Table 2: studies reorganized according to the emotions studied.

5.4 Data Preparation

This section will describe the pre-processing only for papers where extra steps were required. For the other papers we directly extracted the relevant information.

5.4.1 Vannuscorps et al.

From Vannuscorps and colleagues (Vannuscorps et al., 2020) we included the four tasks involving processing of facial expressions (Tasks 1-4). The authors shared raw data, thus we could compute the mean accuracy and standard deviation averaging across different conditions and emotional expressions. Notably, the authors adopted a single-subject analysis method where each MBS was compared to a control group. For experiment 1, 2 and 4 we fitted a multilevel logistic regression and converted the odds ratio for the difference between controls and MBS into a standardized mean difference (see Borenstein et al., 2009). For the experiment 3 we calculated directly the standardized mean difference.

5.4.2 Belluardo et al.

From Belluardo and colleagues (Belluardo et al., 2022) we had access to raw data thus we calculated the mean reaction times and accuracy for MBS and control participants averaging across conditions.

5.4.3 Bate et al.

Similarly to what we did for Vannuscorps et al. (experiment 3) we calculated the summary statistics of the two groups. Given that we did not have access to raw data we calculated the summary statistics of the whole control group using the means and standard deviations of the three reported subgroups.

5.5 Effect size

For each paper and condition we calculated the effect size using the `escalc` function as standardized mean difference (Cohen, 1988; Hedges, 1981) applying the small-sample correction (Hedges, 1981). In particular, we computed the effect size as the difference between control and Moebius participants, divided by the pooled standard deviation. A positive value suggests better performances for controls and thus a deficit for Moebius patients. For raw measures where a lower value represents better performances (e.g., reaction times) we flipped the sign of estimated effect. In particular, we computed the effect size as the difference between control and MBS participants, divided by the pooled standard deviation. A positive value suggests better performance for controls and thus a deficit for MBS patients. For raw measures, where a lower value represents better performance (e.g., reaction times), we flipped the sign of estimated effect.

5.6 Meta-analysis model

We fitted a random-effect meta-analysis model on the data. We used a standard two-level model to reduce the complexity given the limited number of studies and effect sizes. Given that papers could report more than one experiment and/or more than one outcome (e.g., multiple facial expressions) we collapsed the effect sizes and variances with the approach described in Borenstein et al. (2009) and implemented into the `metafor::aggregate()` function. For multiple effect sizes calculated on the same subjects (e.g., different emotions) we collapsed the variances assuming a correlation $\rho = 0.5$ that can be considered plausible given the type of experiments.

When collapsing multiple effect sizes collected on different participants we assumed the sampling errors as independent thus $\rho = 0$. Tests and confidence intervals for the average effect were computed using the Knapp and Hartung method (Knapp & Hartung, 2003). The analysis was carried out using R (version 4.2.3) and the **metafor** package (version 4.0.0) (Viechtbauer, 2010).

5.7 Results

We analyzed a total of $k = 7$ studies. The observed outcomes ranged from 0.147 to 1.083 with 100% of positive results. The estimated average outcome based on the random-effects model is $\beta = 0.381$ ($SE = 0.107$, $95\% CI[0.119, 0.642]$). Therefore, the average outcome significantly differs from zero ($t_6 = 3.556, p = 0.012$). The Figure 5.4 depicts the forest plot of the included studies. Given the number of studies we did not report the publication bias assessment that is discouraged when $k < 10$ (Sterne et al., 2011).

According to the Q-test, there was no significant amount of heterogeneity in the true outcomes. $Q_6 = 8.029$, $p = p = 0.236$, $\tau^2 = 0.022$, $I^2 = 26.622$ %. A 95% prediction interval for the true outcomes is given by -0.064 to 0.825. Hence, although the average outcome is estimated to be positive, in some studies the true outcome may in fact be negative.

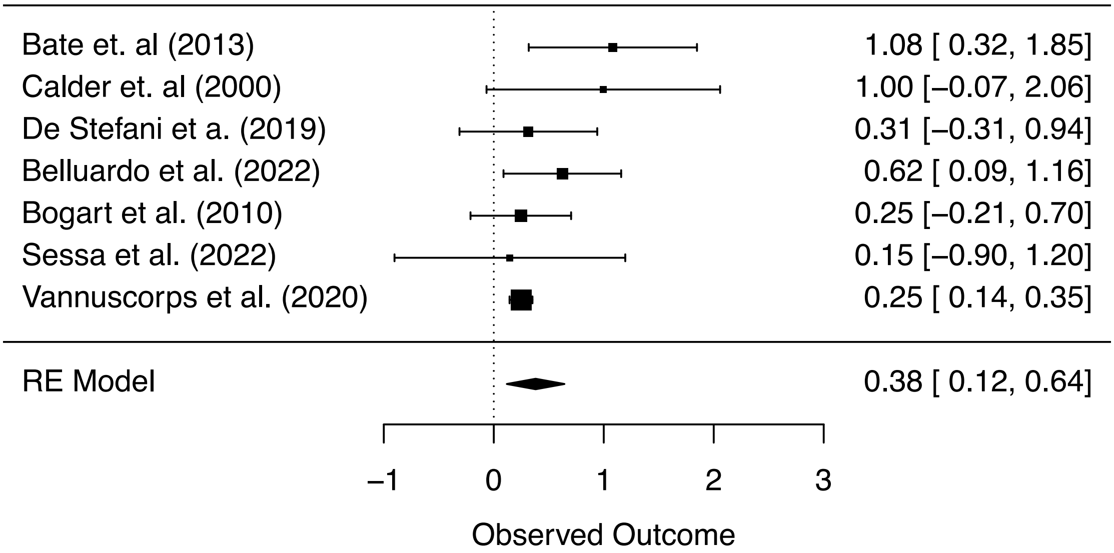


Figure 5.4: Forest plot of included studies. The size of the squares is the inverse-variance weigth of each study. The segments represent the 95% confidence interval. The diamond is the random-effects estimation with the 95% confidence interval.

Chapter 6

Discussion

6.1 Discussion

In accordance with the sensorimotor simulation model, the activation of somatosensory, premotor, and motor neural networks involved in the production of facial expressions would play a functional role in recognizing facial expressions in others (Wood et al., 2016). Neural reactivation might also be accompanied by subthreshold activation of the muscles utilized in the observed expression production. To investigate the model's validity, a series of studies were conducted wherein the facial mimicry of typical subjects was blocked. Research suggests that indeed, when facial mimicry is inhibited, performance in emotion recognition deteriorates (Borgomaneri et al., 2020; Rychlowska et al., 2014; Wood, Lupyan et al., 2016). Moreover, neuroimaging studies appear to indicate that the premotor, somatosensory, and gustatory cortices are among the regions implicated in detecting emotional responses (Kircher et al., 2013; Wicker et al., 2003). Research with individuals suffering from brain lesions has demonstrated the fundamental role of somatosensory-related cortices in recognizing facial expressions (Adolphs et al., 2000; Pourtois et al., 2004).

However, the model could be challenged by contrasting findings observed in research involving patients with Moebius syndrome (MBS), a congenital form of facial paralysis. Since MBS individuals cannot activate facial muscles from birth, they may be unable to utilize the sensorimotor simulation mechanism, consequently resulting in poorer performance than controls in recognizing facial expressions (Sessa et al., 2022). As previously discussed, in some studies (Bate et al., 2013; Belluardo et al., 2022; De Stefani et al., 2019), MBS individuals demonstrate notably inferior performance compared to control groups. Conversely, other studies highlight comparable performance levels (Bogart & Matsumoto, 2010; Calder et al., 2000; Sessa et al., 2022; Vannuscorps et al., 2022).

We consequently decided to conduct a meta-analysis to comprehend the true scale of this effect and any potential impairment in individuals with MBS. We collected all studies involving emotion recognition tasks comparing individuals with MBS to typical controls. It should be noted that the studies are relatively limited in number, totaling only seven, which may result in a less powerful analysis. Nevertheless, an effect size of 0.381 was measured, signifying a small effect (Cohen, 1988). The effect is thus present, though relatively modest. We can hypothesize that individuals with Moebius syndrome are generally less skilled than control subjects in tasks related to emotion recognition.

Returning to the sensorimotor simulation model, the data suggests that simulation likely plays a relatively significant role in facial expression recognition. However, instead of a fundamental role, we could say that it appears to primarily serve as a facilitating factor, simplifying and expediting the recognition process.

Another conclusion that could be drawn is that individuals without facial paralysis may utilize the sensorimotor simulation mechanism, while MBS individuals, owing to congenital paralysis, may have developed alternative mechanisms for facial expression recognition. Indeed, one study has indicated how the processing of facial expressions, which primarily engages the dorsal circuitry in healthy subjects (Duchaine & Yovel, 2015), appears to involve a more ventral circuit in individuals with MBS. Specifically, a crucial role may be played by the anterior temporal lobe face area (ATL-FA), which typically processes features related to facial configuration. It is conceivable that individuals with MBS may utilize configuration processing to interpret facial expressions (Sessa et al., 2022).

It is also possible that the slight deficit found may not be due to the inability to utilize sensorimotor simulation but rather to other factors related to the syndrome that were uncontrolled in the studies reported. Firstly, it could be related to visual domain impairments, evident in nearly 90% of individuals with MBS (Picciolini et al., 2016). Moreover, in rare cases, the syndrome is associated with autistic-like behaviors (0%-5%) and mild mental retardation (9%-15%), which could play a role in emotional recognition. Furthermore, one cannot ignore the difficulties related to social interactions reported by patients, especially experienced during developmental age, which can later lead adults to have social and psychological difficulties (De Stefani et al., 2019). Individuals with facial paralysis are more at risk of experiencing socioemotional problems (Bogart, 2020). Since people with MBS are unable to express emotions promptly when interacting with others, they are sometimes perceived as less socially oriented or even unintelligent. It is also possible to hypothesize that individuals without paralysis may use facial expressions less when interacting with people with facial paralysis, making the latter less "trained" in recognition due to reduced exposure to such stimuli.

As can be observed in the forest plot presented in the results (Figure 5.4), some of the original studies that initially reported no differences between MBS and controls now seem to indicate a small potential effect arising from the deficit. There are different reasons to explain why this might have occurred.

First and foremost, it is essential to emphasize, as also noted in the results, that while the effect appears positive, some of the confidence intervals reported include zero, implying that the true outcome could potentially be negative. Secondly, it is necessary to consider that, for certain studies, both participants and emotion data were aggregated. Regarding emotions, it is possible that individuals with MBS may encounter challenges only in specific expressions and not others, perhaps the finer, less stereotypical ones. When all emotions are collapsed, deficits in a specific type of expressions may have carried more weight. Furthermore, some of the studies adopted a single-subject approach, whereas in our meta-analysis we aggregated individual subject data into a single group, which was then compared to the control group. This is what might have happened, for instance, in the study by Vannuscorps et al. (2020): in the original paper, the analyses were conducted on individual subjects; the more pronounced deficits of certain subjects might have had a more substantial impact when the data were aggregated at the group level.

It is interesting to note that, in some of the studies collected for the analysis, subjects were not required to provide responses within a predefined time frame;

only a few articles took reaction times into account. This could manifest as a performance that appears similar but may have actually required individuals with MBS more time to achieve comparable results to the controls. An example of this is the study by Sessa et al. (2022): while in the meta-analysis we only considered the facial expression morphing task, in the original study subjects also completed an animal morphing task. While controls exhibited shorter reaction times for faces and longer ones for animals, individuals with MBS showed the opposite pattern.

6.1.1 Limitations

In general the results presented above should be interpreted with caution, as the collected studies were few in number and had diverse designs, making comparisons more complex.

Firstly, the small number of studies may have caused the heterogeneity test (which assesses the degree of similarity or dissimilarity among the results from various studies) and the average effect test to be underpowered, generating conclusions that should be taken with caution.

Another limitation of the analysis is the small number of participants in the studies. Given that it concerns a rather rare syndrome, it is quite challenging to recruit participants for this type of research: the majority of the studies included fewer than 10 participants with the syndrome. Additionally, each study employed a different approach in selecting the number of controls to compare with the sample: some studies matched the number of MBS individuals with controls (e.g. Bogart & Matsumoto, 2010), while others had significantly smaller experimental groups compared to controls (e.g. Calder et al., 2000).

The collected studies present rather diverse experimental designs. Some studies employed simple static recognition tests (Bate et al., 2013; Bogart & Matsumoto, 2010; Calder et al., 2000), while others utilized dynamic stimuli, for example instructing subjects to stop the video when the facial expression changed (De Stefani et al., 2019) or to indicate, among two videos, which one depicted a faster change in expression (Belluardo et al., 2022). A few experiments employed morphing tasks, where stimuli resulted from a blend of two expressions in different proportions (Sessa et al., 2022; Calder et al., 2000; Bate et al., 2013). Some studies conducted multiple experiments using various tasks listed. This variability in experimental tasks may have influenced the data collected in individual studies, with some task types potentially more clearly highlighting the deficit than others. Furthermore, while some studies adopted a single-subject approach, others compared a MBS group with a control group. In the study by Bates et al. (2013), for example, there were three experimental groups compared to three control groups matched for age and IQ. Reporting all results as a two-group comparison could, therefore, be imprecise.

In order to obtain a simpler model we opted to aggregate various facial expressions. As mentioned in the preceding paragraph, the results may vary depending on the emotion under investigation. It would have been intriguing to examine individual emotions but, given that each study selected a different set of expressions, this approach would have been complex and would have had reduced statistical power. In fact, some studies included only Happiness and Sadness, while others encompassed all six basic emotions proposed by Ekman (Ekman, 1999), and yet others incorporated more nuanced expressions.

6.1.2 Conclusions

Overall, what this meta-analysis suggests is that there are still many uncertainties regarding individuals with Moebius syndrome and their abilities in recognizing facial expressions. There appears to be a slight deficit, at least in some individuals, but we cannot be certain that it is due to the inability to use sensorimotor simulation. More in-depth studies are needed, which would also involve exploration of other aspects of social interactions in individuals with MBS or employ different stimuli, such as less stereotypical facial expressions.

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*=works not directly consulted

Appendix A

In this appendix you will find the search strings used for literature search. There are three separate tables that show the keyword strings employed in various databases along with their respective outcomes. The databases searched include Web of Science, Scopus and PubMed.

Table a: results in WEB OF SCIENCE

No.	Keywords	Results in Topic (TS)
1	Moebius	870
2	Moebius syndrome	448
3	Moebius OR Moebius syndrome	870
4	Facial feedback hypothesis	236
5	Feedback	559,589
6	Motor simulation	57,694
7	Mimicry	19,441
8	Embodied simulation theory	828
9	Emotion recognition	30,735
10	Emotional processing	68,941
11	Mirror neuron system	3,821
12	Fac*	10,556,577
13	Fac* AND Moebius	278
14	Facial feedback hypothesis OR Feedback OR Motor simulation OR Mimicry OR Embodied simulation theory OR Emotion recognition OR Emotional processing OR Mirror neuron system	726 617
15	(Facial feedback hypothesis OR Feedback OR Motor simulation OR Mimicry OR Embodied simulation theory OR Emotion recognition OR Emotional processing OR Mirror neuron system) AND (Moebius)	15
16	(Facial feedback hypothesis OR Feedback OR Motor simulation OR Mimicry OR Embodied simulation theory OR Emotion recognition OR Emotional processing OR Mirror neuron system) AND (Moebius) AND (Fac*)	15
Total: 15		

Table b: results in SCOPUS

No.	Keywords	Results in article title, abstract, keywords
1	Moebius	1,539
2	Moebius syndrome	1,059
3	Moebius OR Moebius syndrome	1,539
4	Facial feedback hypothesis	215
5	Feedback	761,508
6	Motor simulation	99,918
7	Mimicry	24,057
8	Embodied simulation theory	822
9	Emotion recognition	36,004
10	Emotional processing	33,258
11	Mirror neuron system	2,942
12	Fac*	15,929,183
13	Fac* AND Moebius	791
14	Facial feedback hypothesis OR Feedback OR Motor simulation OR Mimicry OR Embodied simulation theory OR Emotion recognition OR Emotional processing OR Mirror neuron system	942,554
15	(Facial feedback hypothesis OR Feedback OR Motor simulation OR Mimicry OR Embodied simulation theory OR Emotion recognition OR Emotional processing OR Mirror neuron system) AND (Moebius)	19
16	(Facial feedback hypothesis OR Feedback OR Motor simulation OR Mimicry OR Embodied simulation theory OR Emotion recognition OR Emotional processing OR Mirror neuron system) AND (Moebius) AND (Fac*)	19
Total: 19		

Table c: results in PUBMED

No.	Keywords	Results in ALL FIELDS
1	Moebius	719
2	Moebius syndrome	798
3	Moebius OR Moebius syndrome	1,132
4	Facial feedback hypothesis	243
5	Feedback	193,441
6	Motor simulation	15,173
7	Mimicry	15,185
8	Embodied simulation theory	362
9	Emotion recognition	20,194
10	Emotional processing	82,232
11	Mirror neuron system	1,619
12	Face OR Facial	544,442
13	(Face OR Facial) AND ((Moebius syndrome) OR (Moebius))	548
14	Facial feedback hypothesis OR Feedback OR Motor simulation OR Mimicry OR Embodied simulation theory OR Emotion recognition OR Emotional processing OR Mirror neuron system	315,760
15	(Facial feedback hypothesis OR Feedback OR Motor simulation OR Mimicry OR Embodied simulation theory OR Emotion recognition OR Emotional processing OR Mirror neuron system) AND (Moebius)	17
16	(Facial feedback hypothesis OR Feedback OR Motor simulation OR Mimicry OR Embodied simulation theory OR Emotion recognition OR Emotional processing OR Mirror neuron system) AND (Moebius) AND (Face OR Facial)	16
Total: 17		