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Cross-species comparison of behavioral neurodevelopmental milestones in the common marmoset monkey and human child

K. K. Ausderau[1,2,*], **C. Dammann**[1,*], **K. McManus**[3], **M. Schneider**[1,4], **M. E. Emborg**[3,5], and **N. Schultz-Darken**[3]

[1]Occupational Therapy Program, Department of Kinesiology, University of Wisconsin, Madison

[2]Waisman Center, University of Wisconsin, Madison

[3]Wisconsin National Primate Research Center, University of Wisconsin, Madison

[4]Harlow Center for Biological Psychology, University of Wisconsin, Madison

[5]Medical Physics, University of Wisconsin, Madison

Abstract

The common marmoset (*Callithrix jacchus*) is an increasingly popular non-human primate species for developing transgenic and genomic edited models of neurological disorders. These models present an opportunity to assess from birth the impact of genetic mutations and to identify candidate predictive biomarkers of early disease onset. In order to apply findings from marmosets to humans, a cross-species comparison of typical development is essential. Aiming to identify similarities, differences, and gaps in knowledge of neurodevelopment we evaluated peer-reviewed literature focused on the first six months of life of marmosets and compared to humans. Five major developmental constructs, including reflexes and reactions, motor, feeding, self-help, and social, were compared. Numerous similarities were identified in the developmental sequences with differences often influenced by the purpose of the behavior, specifically for marmoset survival. The lack of detailed knowledge of marmoset development was exposed as related to the vast resources for humans.

Keywords

Monkeys; marmosets; *Callithrix jacchus*; human; neurodevelopment; reflexes and reactions; motor; social; feeding; and self-help

1 INTRODUCTION

Non-human primates (NHPs) serve as valuable animal models of human disease. The common marmoset (*Callithrix jacchus*) is an increasingly popular NHP species for developing models of neurological disorders (‘t Hart et al., 2000; Okano, Hikishima, Iriki, &

Corresponding author: Marina E. Emborg, M.D., Ph.D., Preclinical Parkinson’s Research Program, Wisconsin National Primate Research Center, University of Wisconsin - Madison, 1223 Capitol Court, Madison, WI 53715, USA, Phone: 608-262-9714. Fax: 608-263-3524. emborg@primate.wisc.edu.
*both authors contributed equally

Sasaki, 2012; Tardif, Abee, & Mansfield, 2011). Conditions such as Parkinson's disease (Ando et al., 2008; Ando et al., 2012; Gnanalingham, Smith, Hunter, Jenner, & Marsden, 1993; Huot et al., 2012), Huntington's disease (Kendall et al., 1998; Maclean, Baker, Ridley, & Mori, 2000), Alzheimer's disease (Baker, Ridley, Duchen, Crow, & Bruton, 1993) and multiple sclerosis ('t Hart et al., 2000; Genain & Hauser, 1997) have been modeled in marmosets mainly by neurotoxin administration. Advances in the role of genetics in these disorders, as well as in the tools to generate transgenic and genomic edited models, are moving the field towards a new generation of disease models.

Several characteristics of the common marmoset make the species attractive for genetic approaches. Marmosets frequently deliver twins or triplets and have a shorter gestation period than other primates. Additionally, marmosets living in captivity have a shorter lifespan than old world NHPs, an advantage in the study of age-related disorders. Finally, the smaller size and relatively easy temperament of marmosets facilitates their handling, housing, and care (Abbott, Barnett, Colman, Yamamoto, & Schultz-Darken, 2003; Schultz-Darken, Braun, & Emborg, 2016; Tardif et al., 2003; Tardif et al., 2011; Tardif, Mansfield, Ratnam, Ross, & Ziegler, 2011).

Transgenic and genomic edited models present an opportunity to assess from birth the impact of genetic mutations and to identify candidate predictive biomarkers of early disease onset. In order to apply these findings from marmosets to humans, a cross-species comparison of typical development is essential. Prior research of typical marmoset development includes a combination of direct observation and retrospective recall of marmoset behavior (Braun, Schultz-Darken, Schneider, Moore, & Emborg, 2015; de Castro Leão, Duarte Dória Neto, & de Sousa, 2009; Kaplan & Rogers, 2006; Missler et al., 1992; Pistorio, Vintch, & Wang, 2006; Wang, Fang, & Gong, 2014; Yamamoto, 1993). Marmoset development has been based on distinct postnatal stages, though the definitions of these stages differ between research groups; thus, expression of marmoset age in weeks, as opposed to postnatal stage, can be used to avoid ambiguity. Most knowledge of typical marmoset development is concentrated within the first 16–24 weeks of life, prior to the onset of sexual maturity and adulthood.

Although the underlying theoretical perspectives of human development have changed over time, the typical sequence has been well studied and clearly outlined since the 1940s (Gesell et al., 1940; Gesell, 1945; Gesell & Amatruda, 1947). Current theories suggest a complex interaction of biological maturation, engagement, and environmental context explaining detailed progression across developmental constructs (Bronfenbrenner, 1994; Gibson, 1988; Schmidt & Lee, 1988; Wertsch, 2008). The majority of children achieve these developmental milestones in a similar order, often within similar timeframes. Due to the vast knowledge of human development, a multitude of developmental screenings and assessments provide standardized knowledge of pivotal milestones and skills (e.g., Bayley, 2006; Squires, Bricker, & Potter, 1999). These tools allow a means for identification of atypical development associated with various conditions which could eventually lead to the identification of predictors of disease to emerge later in life.

Using the vast preexisting data on human development and the emerging data on the common marmoset development, the purpose of this study is to identify similarities, differences, and gaps in knowledge of the neurodevelopment of the common marmoset as compared to humans. The typical development comparison will provide a foundation for the understanding of normal neurodevelopment and genetic models of child and adult neurological disorders while potentially identifying candidate predictive biomarkers of disease.

2 METHODS

A systematic search for peer-reviewed articles related to developmental timelines in the common marmoset and in humans was conducted in CINAHL and PubMed up to January 2017. Academic databases were searched using key terms such as development, human, child, and marmoset as well as related terms such as reflexes, motor, feeding, social, and behavior. In addition, reference lists, textbooks, and standardized assessments were reviewed for relevant information. Searches were limited to the English language. We included both prospective and retrospective resources with developmental information as primary or secondary outcomes of the research. Limited quantity of relevant documents related to marmoset development were identified. However, a plethora of resources on human development were found, thus references were chosen subjectively based on quality and publication date.

Marmoset references were reviewed initially with identification of developmental milestones and age of skill attainment, primarily focusing on birth to approximately six-months as it is the most rapid period of development in primates (King, 1974; Tardif, 2002). Second, human development resources were reviewed and comparable milestones were identified along with age of skill attainment. In addition, foundation human developmental skills that were unmatched in the marmoset literature were noted. All marmoset and human resources were reviewed independently by at least two team members. Age of skill attainment for both species was rounded to weeks if reported in days. Occasionally, the average age of marmoset skill attainment differed among articles. In this case, the approximate age of attainment from an article based on direct observation of marmoset behavior was prioritized over information based on retrospective questionnaires. Furthermore, the approximate age of attainment for several marmoset skills was extended to reflect similar ranges from multiple articles. The approximate age of attainment for human skills remained fairly consistent across multiple sources.

Team meetings with experts in both marmoset and human development occurred over a period of several months in order to collaboratively identify and review comparable developmental skills in both species. In addition, essential marmoset and foundational human skills that were unmatched in the other species were agreed upon by all team members. Finally, identified skills were reviewed and grouped into major developmental constructs.

3 RESULTS

The systematic search resulted in identification of seven peer-reviewed research articles related to development of the common marmoset. Six articles relied on direct observation of marmoset behavior, while one article used a retrospective questionnaire to describe marmoset development. Human development has been extensively studied and described. As a result, 27 resources related to human development were employed to complete this cross-species comparison; they included peer-reviewed articles, standardized developmental assessments, and renowned textbooks. See Table I for detailed information about bibliography used.

Milestones gathered through the systematic search were organized into five primary developmental constructs, based on categories commonly cited in human developmental research. The constructs were reflexes and reactions, motor (gross and fine), feeding, self-help, and social skills. Reflexes included automatic, involuntary responses to stimuli, while reactions encompassed automatic responses which function to keep the body upright. Motor skills were considered as large (gross) movements important in ambulation and small (fine) movements critical in precise manipulation of objects. Feeding skills consisted of behaviors to support the attainment of proper nutrition. Self-help skills supported independent functioning and self-reliance. Finally, social skills included behaviors that support communication (e.g., visual skills) and interaction with other members of the species (e.g., reproductive development).

Two important developmental constructs, vocalizations and cognition, are not reported in the results of this comparison. The first, vocalizations, is highly complex in marmosets; as a result, the topic was deemed too specific for this broad developmental comparison. The second, cognition, is not yet well studied or understood in the developing common marmoset. In contrast, cognition is highly developed, complex, and widely studied in humans.

Results presented in Tables II–VI, which are organized by developmental construct, identified marmoset skills and approximate age of skill attainment. Related human skills and approximate age of attainment are to the right of each marmoset skill. The bottom of each table includes essential marmoset skills and/or foundational human skills unmatched between species (either not present or not documented). Several skills can be found in more than one table, as their purposes meet criteria of multiple developmental constructs. For example, self-feeding and finger feeding are found in Tables IV and V, as they are important feeding and self-help skills.

Table II compares typical developmental reflexes and reactions in marmosets and humans. To date, the studied spectrum of reflexes and reactions in marmosets have been limited. Reflexes and reactions in marmosets have primarily been examined within the first month of life (Braun et al., 2015); as a result, the age at which these responses are inhibited has not been identified in our review. Of note, reflexes such as the palmar and plantar grasp and the rooting response are present in both species around birth. Further study of the sucking and pharyngeal reflexes in marmosets would provide valuable insight into feeding similarities between the species.

Typical developmental gross and fine motor skills are outlined in Table III. Many similarities exist between gross motor development in marmosets and humans. Independent mobility in both species begins with crawling before advancing to walking and running. However, marmosets display jumping and climbing behaviors earlier in life than humans, likely due to the arboreal nature of the species. Figure 1 shows side by side marmoset and human climbing. In addition, while similarities exist between aspects of movement patterns such as geotaxis, their early emergence for survival in marmosets is essential. For example, early in life young marmosets must understand how to negotiate getting off and on their caregivers and proper physical positioning. Human infants do not develop that skill until they begin negotiating changes in positions, crawling, or climbing up stairs. Fine motor skills are important to independent feeding in both species. In marmosets, the ability to hold onto the carrier’s back is an essential survival skill, as this is the primary form of mobility in early life. Development of fine motor skills in humans is well outlined, as these skills are essential for playing, learning, and socialization. The same level of description is not available in marmosets at this time.

Table IV illustrates many similarities between the development of feeding skills in marmosets and humans. Both species nurse at birth in order to obtain essential nutrients for growth and survival. Similarly, both begin to eat solid foods during the weaning period, prior to cessation of nursing or bottle feeding. The ability to capture living prey is a feeding skill essential to marmoset survival, which is unmatched in human development. Another important unmatched skill for marmosets, particularly in the wild, is tree gouging. Marmosets use their incisors to chew holes through tree bark to feed on the sap or energy rich gum (Lacher, da Fonseca, Alves, & Magalhaes-Castro, 1981). Figure 2 shows examples of feeding behaviors in marmosets and human children.

Table V compares developmental self-help skills, many of which are similar in marmosets and humans. Both species display self-mouthing and self-calming behaviors relatively early in life. Physical independence is accompanied by spontaneous exploration of the environment and expression of the desire for autonomy in both species. Marmosets, however, display self-grooming behavior earlier in life than humans.

Typical developmental social skills are outlined in Table VI. Both species display visual orientation and visual following early in development to support a number of motor skills and allow engagement in social interactions. Marmosets and humans engage in solitary play before social play in groups. However, humans develop their ability to engage in quality social interactions with individuals and groups sequentially, while these types of individual and group social skills unfold simultaneously in marmosets. Scent marking in marmosets begins earlier in development than human protection of toys. The purpose of scent marking in marmosets is protection of space and feeding resources (i.e., tree gouging behavior) between family groups versus within a family. Social grooming is an important skill in marmosets that serves a primary social purpose versus hygiene, often beginning between a parent and infant. Although social grooming is not named in human dyads, early in life there are many parent-child daily hygiene activities (e.g., bathing, diapering) that support social connection and bonding (O'Brien & Lynch, 2011) similar to marmosets. See Figure 3.

4 DISCUSSION

4.1 Marmoset vs. Human

The cross-species comparison of typical development in the marmoset and human allowed us to begin to understand their similarities and differences while identifying important gaps in knowledge. Currently, there is a dearth of information in the literature comparing these two species even though the knowledge could serve a pivotal role in early assessment of genetic mutations and identification of predictive biomarkers of early disease onset.

Although marmosets and humans share significant aspects of their genome, they have distinct anatomical and biological differences underlying their divergent evolutionary development. In 2014, the marmoset genome was mapped and sequenced which has facilitated comparison with humans and other species to explain the emergence of specific traits such as twinning, and small size of the species (Harris et al., 2014; The Marmoset Genome Sequencing & Analysis Consortium, 2014). With respect to neuroanatomy, marmosets like other non-human primates, have a lissencephalic brain, albeit smaller. The lateral or sylvian fissure, temporal lobes, internal structures and neuroanatomical organization of the marmoset brain is similar to other primate brains, including humans (Hashikawa, Nakatomi, & Iriki, 2015; Hikishima et al., 2013; Hikishima et al., 2011; Newman et al., 2009). However, marmosets are a unique NHP species in that they are distinguished by small body size, narrow dental formula, claws on all digits except a specialized nail (hallux) on the first digit of each foot, which is the only opposable joint, and specialized scent glands in the chest and genital areas (Garber, 1992; Magden, Mansfield, Simmons, & Abee, 2015; Natori & Shigehara, 1992). These adaptations reflect the arboreal lifestyle and tree exudate diet. The anatomical similarities and differences between the common marmoset and humans should be considered as development between the species is compared. Average global human lifespan is 71.4 years (World Health Organization, 2016) while the average marmoset lifespan in captivity is 5–7 years (Tardif et al., 2011) with a maximum lifespan in captivity of about 16 years (Schultz-Darken et al, 2016). In this context, marmosets have an accelerated developmental timeline and by four to seven months of age they are already considered juveniles (de Castro Leão et al., 2009).

In the following paragraphs, we discuss differences and similarities, purpose of behaviors, and unmatched skills within the five developmental constructs. We highlight specific marmoset and human behaviors that illustrate these points.

4.2 Reflexes and Reactions

Several reflexes and reactions which are essential to survival have been identified in the common marmoset that are equivalent in humans. Plantar and palmar grasp reflexes are essential to marmoset survival, as they play an important role in the ability to cling to the caregiver's back. The rooting response, critical for nursing, is present early in life in both humans and marmosets. To date, limited studies of reflexes and reactions in the common marmoset have been published. Knowledge of these responses is primarily limited to the first four weeks of life with limited information available regarding inhibition of reflexes in the common marmoset. Alternatively, human reflexes have been widely studied. Inhibition of reflexes is well-documented, as persistence of reflexes beyond a certain age is often a sign of neurological damage (Zafeiriou, 2004). Study of older marmosets would provide valuable information regarding inhibition of reflexes and reactions essential to survival. Furthermore, several important reflexes in human development, such as the pharyngeal reflex and asymmetric tonic neck reflex, have not been studied in marmosets. An expanded understanding of reflexes and reactions in the common marmoset would allow for a more comprehensive comparison between marmoset and human development.

4.3 Motor Skills

A number of important motor skills emerge relatively earlier in marmoset than human development, at least partially necessitated by their arboreal lifestyle. For example, marmosets are able to crawl, jump, climb, and run much earlier in life than humans. The arboreal nature of the marmoset requires these skills to develop at a young age to enable independent exploration of the environment and survival of the species. These motor skills usually emerge later in human development, as they do not play such an essential role in early survival. While the same skills are important in human development, they serve as building blocks to support other skill development, rather than survival mechanisms. One essential marmoset skill that is unmatched in human development plays a similar role to the aforementioned skills. The ability to hold onto the carrier’s back and use negative geotaxis to orient the body while being carried is present from birth in the marmoset and critical to survival. Several skills outlined in human development, such as the pincer grasp and transferring objects between hands, have not been documented in marmosets. While these skills are likely present in marmosets (with the caveat that the pincer grasp is only present in their feet) they do not represent the pivotal milestones they do in humans.

4.4 Feeding Skills

Development of feeding skills in marmosets and humans share many similarities. Both species obtain nutrition via nursing or breastfeeding prior to progressing to solid foods, with marmosets reaching those milestones slightly earlier. Of note, the ability to capture living prey is an essential survival skill in marmosets living in the wild that is unmatched in humans. The emergence of this skill at a young age of eight to nine weeks is a reflection of necessity for independent retrieval of nutrition early in life. In contrast, humans are not expected to independently obtain or prepare food until much later in life. One important skill in human development that has not been documented in marmosets is the recognition of a bottle by sight. However, marmosets do allow group members close proximity in feeding and share food without opportunity for reciprocity (Burkart, Fehr, Efferson, & van Schaik, 2007), which allows younger animals the ability to identify and seek out proper food items from other group members.

4.5 Self-help Skills

Development of self-help skills in marmosets resembles human development in several ways. Both species display self-mouthing, or bringing the hands to the mouth, early in development. This skill is an important precursor to the ability to self-feed, which is essential to independence from caregivers in both species. Auto-grooming, environmental exploration, and physical independence emerge relatively early in marmoset development, all of which contribute to the early independence observed in the species. The ability to capture living prey is an essential self-help skill in marmosets that is unmatched in humans. As previously discussed, the ability to independently obtain nutrition at a young age is required for marmoset survival in the wild, but is typically not necessary to human survival until much later in life. Refusal of excess food is an important skill in humans for appropriate growth and nutrition, which has not been documented in marmosets, though the skill is likely present in the latter species. Regarding self-help, a number of important human developmental skills such as spoon-feeding and dressing, are unmatched in marmosets as they are not relevant to the species.

4.6 Social Skills

Social development in marmosets and humans share many similarities, due to the tendency of marmosets to pair-bond, live in family groups with cooperative care of the young, practice food-sharing, and learn by imitation in a similar manner to humans (Miller et al., 2016). Both species display distinct cries indicating distress early in development. Furthermore, both species display consolability relatively early in development, reflecting the ability of young marmosets and human infants to regulate behavior based on caregiver responses. However, marmosets live in family groups allowing for a great number of family members to routinely respond to and regulate young marmosets. In human Western cultures, immediate family members, typically the parents, are often primary caregivers with extended family members helping less frequently.

Head cocking is an important social skill that emerges early in marmoset development; this skill is related to the visual tracking that emerges early in human development. Both skills are essential to early visual exploration and learning. Play follows a similar progression in both species, beginning with solitary play and gradually expanding to include social play with peers. The manifestation of agonistic behaviors differs significantly between marmosets and humans. Marmoset displays of agonism include scent marking, piloerection, and baring of the teeth (de Boer, Overduin-de Vries, Louwerse, & Sterck, 2013); these behaviors are often related to protection of food sources (Lazaro-Perea, Snowdon, & de Fátima Arruda, 1999; Lazaro-Perea, 2001). Agonistic behaviors in humans, specifically physical aggression, may have evolved from similar territorial behaviors. Social grooming is another important developmental skill in marmosets. Although the unique behavior is unmatched in human relationships, parent-child dyads participate in many similar grooming type activities (e.g., bathing, diapering) that contribute to dyad bonding and support infant hygiene (O’Brien & Lynch, 2011). Caregiver recognition and joint attention are important human developmental milestones that have not been documented as such in marmosets. However, marmoset behaviors such as nursing, food sharing, and social grooming imply similar skill attainment early in marmoset development as well.

4.7 Limitations of this Study and Future Directions

The current paper offers a cross-species comparison of early development and underscores the limited knowledge about the developing marmoset compared to the extensive and detailed knowledge of human development. Although a direct comparison of monkeys versus humans could be more informative, for the purpose of this project we chose a literature review of marmoset development in order to 1) analyze current available knowledge in the literature, 2) expand data beyond one monkey colony, and 3) compare human vs marmoset development using similar data mining strategies.

Human development studies began in the nineteenth century. In comparison, the first general report of marmoset behaviors was published in 1976 (Stevenson & Poole), further highlighting the infancy of marmoset developmental studies. Overall, there continues to be limited opportunities for marmoset observation with only three National Institutes of Health (NIH) sponsored captive colonies (two National Primate Research Centers and one NIH intramural colony) in the United States (National Primate Research Centers, n.d.). A few additional scattered captive populations also exist within laboratories in the United States and around the world such as in Brazil, Ecuador, Germany, and Japan. Of the seven original research papers found in marmoset development, one foundational study was retrospective and based on a questionnaire, which should be taken into consideration when examining the results (Missler et al., 1992). The number of subjects per study was relatively small ranging from 9 to 24 marmosets; additionally, two studies did not report the specific number of subjects (de Castro Leão et al., 2009; Missler et al., 1992). A combination of novelty and opportunity has limited research, yet the unfolding of marmoset development has become an increasing priority for future work as researchers aim to assess whether neurodevelopmental challenges emerge early in neurodegenerative disorders and whether that can be compared to humans.

Many of the marmoset observations took place in captive or laboratory environments. The extent to which the context of the marmoset observation affects the animals' unfolding development (e.g.: captive vs. wild; laboratory vs. natural environment) is not clear. However, we do know that certain behaviors such as feeding on and defending gum exudate trees or an equivalent behavior are only observed in wild populations (Lazaro-Perea, 2001). Other behaviors persist in laboratory environments; for example, marmosets housed in family groups in the laboratory naturally give rise to rich social interaction and most species-typical behaviors (Stevenson & Poole, 1976). Future studies will need to assess how environmental affordances may shape early marmoset development.

For the goal of this article, the identification and characterization of the behaviors can be used as the foundation to understand normal behavior and cognition, evaluate novel genetic-based models, and help in the detection of early developmental markers of disease. Future marmoset research should explore additional developmental constructs (e.g., cognition), age for extinction of reflexes, and extend the comparison into adolescent and adult age ranges. Similar to humans, the success of marmosets achieving neurodevelopmental milestones provides insight into the overall health and well-being of the animals. As such, marmoset studies aiming to fulfill gaps in knowledge will benefit animal care, investigations on genetic models and treatments, and ultimately, humans.

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Figure 1.

Early mobility skills in a marmoset and humans. **(A)** A young marmoset (~2 months) orients to begin moving up an inclined surface, as compared to **(B)** two young children (14 months) creeping up stairs. Marmosets begin orienting and moving up a plane at 4 weeks, while humans begin creeping up stairs at 14 months.

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Figure 2.
Eating behaviors in marmosets and humans. **(A)** A juvenile marmoset eats a cookie, as compared to **(B)** a young child (18 months). Self-feeding skill typically emerges in marmosets around 4–12 weeks, while finger feeding in humans begins around 7–9 months. **(C)** A young marmoset (~3 months) engages in tree gouging for exudate, as compared to **(D)** a young child self-spoon feeding (18 months). Marmosets begin tree gouging for exudate around 12–16 weeks, while humans begin self-spoon feeding around 12 months.

Figure 3.

Social grooming in marmosets and humans. **(A)** A marmoset father is holding an infant (~1 month old) while being groomed by another adult member of the group, as compared to **(B)** a human parent bathing an infant (1 week old). Marmosets begin social grooming around 16–28 weeks. While not specifically labeled social grooming, humans frequently engage in dyadic activities related to grooming, such as bathing and diapering.

Table I

Characteristics Of The Bibliography Used For The Comparison Of Common Marmoset Monkeys And Humans Neurodevelopment

Marmosets

Reference	Peer Review (PR)/ Textbook (T)	Retrospective (R)/Prospective (P)	Number of Subjects
Braun, Schultz-Darken, Schneider, Moore, & Emborg, 2015	PR	P	24
de Castro Leão, Duarte Doria Neto, & de Sousa, 2009	PR	R	Not Reported
Kaplan & Rogers, 2006	PR	P	15
Missler et al., 1992	PR	R	Not Reported
Pistorio, Vintch, & Wang, 2006	PR	P	9
Wang, Fang, & Gong, 2014	PR	P	11
Yamamoto, 1993	PR	P	9 (*Callitrichid genera*; n=4 and *Callithrix jacchus*; n=5)

Humans

Reference	Peer Review (PR)/ Textbook (T)	Retrospective (R)/Prospective (P)	Number of Subjects
American Academy of Pediatrics, 2009	T	N/A	N/A
Bayley, 2006	T	N/A	N/A
Bretherton, 1980	T	N/A	N/A
Case-Smith, 2015	T	N/A	N/A
Child development tracker, n.d	N/A	N/A	N/A
Côté, Vaillancourt, LeBlanc, Nagin, & Tremblay, 2006	PR	P	10,658
Delaney & Arvedson, 2008	PR	N/A*	N/A
Edwards, Buckland, & McCoy-Powlen, 2002	T	N/A	N/A
Folio & Fewell, 2000	T	N/A	N/A
Fuller, 1991	PR	P	21
Futagi & Suzuki, 2010	PR	N/A*	N/A
Gahagan, 2012	PR	N/A*	N/A
Gallahue, Ozmun, & Goodway, 2012	T	N/A	N/A
Gartner et al., 2005	PR	N/A	N/A
Gerber, Wilks, & Erdie-Lalena, 2010	PR	N/A*	N/A
Knox, 1997	T	N/A	N/A
Korth & Rendell, 2015	T	N/A	N/A
Lewis, 2006	T	N/A	N/A
Mandich, 2015	T	N/A	N/A
Mathiowetz & Haugen, 1995	T	N/A	N/A
Mulligan, 2013	T	N/A	N/A
Neelon & Harvey, 1999	PR	N/A	N/A

Marmosets			
Reference	**Peer Review (PR)/ Textbook (T)**	**Retrospective (R)/Prospective (P)**	**Number of Subjects**
Singh, Mukhopadhyay, Rao, & Viswanath, 2013	PR	R	120
Tremblay et al., 2004	PR	P	504
Vroman, 2015	T	N/A	N/A
World Health Organization & UNICEF, 2003	N/A	N/A	N/A
Wright, Cameron, Tsiaka, & Parkinson, 2011	PR	P	602

Key:

* = review article

Table II

Typical Developmental Reflexes and Reactions of Common Marmoset Monkeys and Humans

Marmoset Skill	Marmoset Age	Related Human Skill	Human Age
Plantar grasp	Observed at 2 wks., persists at 4 wks.[1]	Babinski reflex (fanning toes) Plantar grasp reflex (flexion of toes)	Present at birth, inhibited by 36 mos.[2] Initiated at 25 wks. gestation, inhibited at 6 mos.[3]
Labyrinthian righting	Observed at 2 wks., persists at 4 wks.[1]	Labyrinthine righting (without vision) Optical righting	Initiated at 2 mos., persists[4] Initiated at 2 mos., persists[4]
Palmar grasp	Observed at 2 wks., stronger at 4 wks.[1]	Palmar grasp reflex	Initiated at 30 wks. gestation, inhibited at 2 mos.[5]
Suckling reflex	Present at birth[6]	Sucking reflex	Initiated at 28 wks. gestation, inhibited at 3–7 mos.[5]
Rooting response	Observed at 2 wks., stronger at 4 wks.[1]	Rooting reflex	Initiated at 28 wks. gestation, inhibited at 3–7 mos. (may last longer in babies who are nursed)[5]
Parachute response during headfirst descent towards surface	Observed at 2 wks., stronger at 4 wks.[1]	Forward protective response	Initiated 6–7 mos., persists[5]
Body righting from supine to prone	Observed at 2 wks., stronger at 4 wks.[1]	Rolls back to front Body righting reflex	5 mos.[7] Initiated at 6 mos., inhibited at 18 mos.[8]
Galant's response	Observed at 2 wks., stronger at 4 wks.[1]	Trunk incurvation reflex	Present at birth, inhibited at 4–6 mos..[9]
Unmatched Developmental Reflexes and Reactions			
NR	--	Pharyngeal reflex	Initiated at 34 wks. gestation, persists[10]
NR	--	Spontaneous stepping reflex	Initiated at 35 wks. gestation, inhibited at 3 mos.[5]
NR	--	Asymmetric tonic neck reflex	Initiated at 1 mo., inhibited at 4 mos.[5]

KEY: wks.=weeks, mos.=months; NR = not reported; NP= not present

REFERENCES:

[1] Braun, Schultz-Darken, Schneider, Moore, & Emborg, 2015;

[2] Neelon & Harvey, 1999;

[3] Futagi & Suzuki, 2010;

[4] Mathiowetz & Haugen, 1995;

[5] Mulligan, 2014;

[6] Missler et al., 1992;

[7] Gerber, Wilks, & Erdie-Lalena, 2010;

[8] Gallahue, Ozmun, & Goodway, 2012;

[9] Lewis, 2006

[10] Mandich, 2015

Table III

Typical Developmental Motor Skills of Common Marmoset Monkeys and Humans

Marmoset Skill	Marmoset Age	Related Human Skill	Human Age
Gross Motor			
Dependence on caregiver for carrying	Birth-4 wks.[1, 2]	Carrying is primary form of mobility until infant begins rolling and/or crawling	Birth-6 mos. (significant familial, cultural influence)[3]
Raises head and looks up	1–2 wks.[4]	Lifts head to look around	4 mos.[3]
Crawls	1–3 wks.[4]	Crawls on belly Creeps on hands and knees	8 mos.[5] 9–10 mos.[5]
Brief periods "off" caregiver during which infant explores environment through solitary play*	2–4 wks.[2]	Uses familiar caregiver as secure base from which to explore environment* Once mobile, explores environment but continues to maintain proximity to caregiver*	3–6 mos.[3] 12–24 mos.[3]
Sustained semi-flexion of head in prone	2 wks.[6]	Chin up in prone Holds head at 45° then lowers with control in prone Holds head at 90° then lowers with control in prone	1 mo.[5] 4–7 mos.[7] 5–7 mos.[7]
Sustained semi-flexion of head in supine	2 wks.[6]	Turns head when supine	1 mo.[5]
Negative geotaxis			
Holds onto plane	2–3 wks.[4]		
Orients/moves up plane	4 wks.[4]	Creeps up stairs	14 mos.[8]
Stands with forelimb support	3 wks.[4]	Begins standing unsupported	11–12 mos.[5]
Walks	4 wks.[4]	Walks with two hands held Walk with one hand held Walks independently	10 mos.[5] 11 mos.[5] 13–14 mos.[5]
Jumping			
Displays take-off posture	3 wks.[4]	Bends knees to squat, then returns to standing	13 mos.[8]
Jumps	5 wks.[4]	Jumps forward 4 inches	24 mos.[8]
Climbing			
Holds onto rod	3 wks.[4]	Swings from arms when climbing on playground	48–60 mos.[3]
Climbs up rod	8 wks.[4]	Supports weight for several seconds when hanging or climbing, coordinates limbs to propel body	96–108 mos.[9]
Barrier crossing			

Marmoset Skill	Marmoset Age	Related Human Skill	Human Age
Stands on barrier	4 wks.[4]	Crawls over small obstacles	8–12 mos.[10]
Crosses barrier	8 wks.[4]	Climbs on variety of obstacles Walks up stairs	12–24 mos.[3] 15–16 mos.[8]
Runs	6 wks.[4]	Begins running True running pattern	24 mos.[3] 36–48 mos.[3]
Begins leaving spontaneously due to infant attempts and caregiver rejection*	5–10 wks.[2]	Expression of desire for autonomy*	24 mos.[3]
Physically quite independent, carrying ceases*	12–16 wks.[2]	Well-coordinated, balanced gait*	24 mos.[3]
Fine Motor			
Reach and grasp – reaches for toy	Emerging at 4 wks.[6]	Reaches persistently Reaches/grasps hanging toys Changes direction of reach midstream Reach is smooth and efficient in all directions	4 mos.[5] 5 mos.[5] 6–9 mos.[3] 8–9 mos.[3]
Self-feeding*	4–12 wks.[1, 2]	Finger feeding*	6–8 mos.[11]
Eats solid foods unaided*	12–16 wks.[2]	Manages variety of solid foods with complex chewing patterns*	24–36 mos.[12]
Unmatched Developmental Motor Skills			
Holds onto carrier's back	Birth-8 wks.[13]	NP	--
NR	--	Symmetric movements of sides of body	3–6 mos.[7]
NR	--	Holds head in midline when supine	4–7 mos.[7]
NR	--	Transfers objects from hand to hand	6 mos.[5]
NR	--	Sits well without support	7 mos.[5]
NR	--	Pincer grasp develops	10–12 mos.[14]

KEY: wks.=weeks; mos.=months; mo.=month; NR = not reported; NP= not present;

* indicates skill present in multiple tables

REFERENCES:

[1] de Castro Leão, Duarte Doria Neto, & de Sousa, 2009;

[2] Yamamoto, 1993;

[3]Case-Smith, 2015;

[4]Wang, Fang, & Gong, 2014;

[5]Gerber, Wilks, & Erdie-Lalena, 2010;

[6]Braun, Schultz-Darken, Schneider, Moore, & Emborg, 2015;

[7]Bayley, 2006

[8]Folio & Fewell, 2000;

[9]Child development tracker, n.d.;

[10]American Academy of Pediatrics, 2009;

[11]Wright, Cameron, Tsiaka, & Parkinson, 2011;

[12]Korth & Rendell, 2015;

[13]Missler et al., 1992;

[14]Edwards, Buckland, & McCoy-Powlen, 2002

Table IV

Typical Developmental Feeding Skills of Common Marmoset Monkeys and Humans

Marmoset Skill	Marmoset Age	Related Human Skill	Human Age
Nursing	Birth-4 wks.[1]	Exclusive breastfeeding recommended Continued breastfeeding in addition to complementary foods	Birth-6 mos.[2, 3, 4] Until 12–24 mos.[2, 3, 4]
Suckles each hour	1–6 wks.[5]	Cluster feeding	Begins at birth, end highly dependent on culture, family, and growth of the infant[2]
Eats solid foods	4–12 wks.[1]	Begins to eat thin purees Introduction of complementary foods	6 mos.[6] 6 mos.[2, 3, 4]
Self-feeding *	4–12 wks.[1]	Finger feeding *	6–8 mos.[7]
Weaning	5–10 wks.[8]	Continued breastfeeding in addition to complementary foods	Until 12–24 mos.[2, 3, 4]
Nursing ceases, weaning completed	12–16 wks.[1, 8]	Discontinues breastfeeding	12–24 mos. (significant familial, cultural influence)[2, 3, 4]
Eats solid foods unaided and tree gouging for exudate	12–16 wks.[8]	Manages variety of solid foods with complex chewing patterns	24–36 mos.[9]
Unmatched Developmental Feeding Skills			
Able to capture living prey *	8–9 wks.[5]	NP	--
NP	--	Recognizes bottle by sight	4–6 mos.[6]
NP	--	Holds bottle independently	7–9 mos.[6]
NP	--	Drinks from cup	7–9 mos.[6]

KEY: wks.=weeks; mos.=months; NR = not reported; NP= not present;

* indicates skill present in multiple tables

REFERENCES:

[1] de Castro Leão, Duarte Doria Neto, & de Sousa, 2009;

[2] Gartner et al., 2005;

[3] World Health Organization & UNICEF, 2003;

[4] Gahagan, 2012;

[5] Missler et al., 1992;

[6]Delaney & Arvedson, 2008;

[7]Wright, Cameron, Tsiaka, & Parkinson, 2011;

[8]Yamamoto, 1993;

[9]Korth & Rendell, 2015

Table V

Typical Developmental Self-help Skills of Common Marmoset Monkeys and Humans

Marmoset Skill	Marmoset Age	Related Human Skill	Human Age
Self-mouthing	2 wks.[1]	Brings hands to mouth	3 mos.[2]
Auto-grooming	2–3 wks.[3]	Washes hands with supervision Brushes teeth with supervision	24–48 mos.[4] 48–60 mos.[4]
Brief periods "off" caregiver during which infant explores environment through solitary play*	2–4 wks.[5]	Uses familiar caregiver as secure base from which to explore environment* Once mobile, explores environment but continues to maintain proximity to caregiver*	3–6 mos.[6] 12–24 mos.[6]
Self-calming behavior	4 wks.[1]	Develops strategies to calm self when upset	3–6 mos.[4]
Self-feeding*	4–12 wks.[7]	Finger feeding*	7–9 mos.[8]
Begins leaving spontaneously due to infant attempts and caregiver rejection*	5–10 wks.[5]	Expression of desire for autonomy*	24 mos.[6]
Independent locomotion	4–12 wks.[7]	Efficient crawling on multiple surfaces Walks independently	10–12 mos.[6] 13–14 mos.[2]
Physically quite independent*	12–16 wks.[5]	Well-coordinated, balanced gait enables increasingly independent exploration of environment*	24 mos.[6]
Unmatched Developmental Self-help Skills			
Able to capture living prey*	8–9 wks.[3]	NP	--
NR	--	Refuses excess food	7 mos.[2]
NP	--	Self-spoon feeding begins	12 mos.[9]
NP	--	Cooperates with dressing	11 mos.[2]

KEY: wks.=weeks; mos.=months; NR = not reported; NP= not present;

* indicates skill present in multiple tables

REFERENCES:

[1]Braun, Schultz-Darken, Schneider, Moore, & Emborg, 2015;

[2]Gerber, Wilks, & Erdie-Lalena, 2010;

[3]Missler et al., 1992;

[4]Mulligan, 2013;

[5] Yamamoto, 1993;

[6] Case-Smith, 2015;

[7] de Castro Leao, Duarte Doria Neto, & de Sousa, 2009;

[8] Wright, Cameron, Tsiaka, & Parkinson, 2011;

[9] Korth & Rendell, 2015

Table VI

Typical Developmental Social Skills of Common Marmoset Monkeys and Humans

Marmoset Skill	Marmoset Age	Related Human Skill	Human Age
Interaction with caregivers			
Interchange between mom and dad	Birth-8 wks.[1]	Prefers familiar caregivers Prefers primary caregiver with whom attachment has been formed	3–6 mos.[2] 6–36 mos.[2]
Infant distress call, or "Cry"	Shortly after birth-11 wks.[3]	Possible acoustic differentiation in cries related to hunger, pain, fussiness, and wet diaper	Birth-4 mos.[4,5]
Interchange between all group members	1–4 wks.[1]	Responds similarly to any caregiver	Birth-3 mos.[2]
Spends more time on dad than mom	2–4 wks.[6]	Begins to display separation anxiety and preference for specific caregiver	6 mos.[2, 7]
Brief periods "off" caregiver during which infant explores environment through solitary play*	2–4 wks.[6]	Uses familiar caregiver as secure base from which to explore environment* Once mobile, explores environment but continues to maintain proximity to caregiver*	3–6 mos.[2] 12–24 mos.[2]
Consolability	4 wks.[8]	Calms in response to parent or soothing voice	4 mos.[9]
Begins leaving spontaneously due to infant attempts and caregiver rejection*	5–10 wks.[6]	Expression of desire for autonomy*	24 mos.[2]
Relationship with caregiver is stable	18–22 wks.[6]	Understands caregivers will return, increasing flexibility in relationship with caregivers Relationships with adults typically strengthen during transition from adolescence to adulthood	36 mos.[2] 17–21 yrs.[10]
Open-mouth face (affiliative behavior)	4–12 wks.[11]	Social smile	6 wks.[9]
Agonistic behaviors			
Scent marking	Birth-4 wks.[11]	Protective of toys	12–36 mos.[13]
Piloerection begins	4–12 wks.[11]	Protective of toys	12–36 mos.[13]
Bared teeth gecker	< 5 months[12]	Physical aggression (hitting, biting, kicking, fighting, bullying others)	Appears 12–24 mos., peak 24–48 mos.[14, 15]
Visual and auditory development			
Head cocking commences	2–4 wks.[16]	Visually tracks object 12 inches from face 90 degrees to once side of midline Visually tracks object 12 inches from face across midline	1 mo.[17] 2 mos.[17]
Visual orientation	4 wks.[8]	Looks at objects with high contrast Regards toys	1 mo.[9] 3 mos.[9]
Visual following	4 wks.[8]	Visually tracks faces and toys Visually tracks person moving across room	1–3 mos.[9] 3 mos.[9]

Marmoset Skill	Marmoset Age	Related Human Skill	Human Age
Startles to auditory input	4 wks.[8]	Startles to voice/sound	1 mo.[9]
Play			
Predominant solitary play	5–10 wks.[6]	Solitary play predominates	Until 18 mos.[18]
Grooming and social play occasionally	5–10 wks.[6]	Social, parallel play begins	24–30 mos.[2]
Social play predominates	12–16 wks.[11]	Associative play in groups	36–48 mos.[18]
Trend towards interaction with other group members besides parents	22–40 wks.[6]	Cooperative play with peers to reach common goals	48–60 mos.[18]
Reproductive development			
Increase in female estradiol	16–28 wks.[11]	Puberty onset (females)	8–13 yrs.[10]
Male increase in testicular size and testosterone level	28–40 wks.[11]	Puberty onset (males)	11–12 yrs.[10]
Unmatched Developmental Social Skills			
Reproductive development			
Start genital display	12 wks.[1]	NP	--
Grooming			
Social grooming	16–28 wks.[11]	NP	--
Grooming is most common activity	18–22 wks.[4]	NP	--
NR	--	Recognizes caregiver by sight	5 mos.[9]
NR	--	Visually follows pointing, engages in joint attention	9 mos.[9]
NP	--	Gives object to adult to communicate need for help	11 mos.[9]

KEY: wks.=weeks; mos.=months; mo.=month; yrs.=years; NR = not reported; NP= not present;

[*]indicates skill present in multiple tables

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