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Cognitive and motor aging in female chimpanzees

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ABSTRACT

We present the first longitudinal data on cognitive and motor aging in the chimpanzee (*Pan troglodytes*). Thirty-eight adult female chimpanzees (10–54 years old) were studied. The apes were tested longitudinally for 3 years in a modified Primate Cognition Test Battery, which comprised 12 tests of physical and social cognition. The chimpanzees were also administered a fine motor task requiring them to remove a steel nut from rods of various complexity. There was little evidence for an age-related decline in tasks of Physical Cognition: for most tasks, performance was either stable or improved with repeated testing across age groups. An exception was Spatial Memory, for which 4 individuals more than 50 years old experienced a significant performance decline across the 3 years of testing. Poorer performance with age was found in 2 tasks of Social Cognition, an attention-getting task and a gaze-following task. A slight motor impairment was also observed, with old chimpanzees improving less than younger animals with repeated testing on the simplest rod. Hormonal status effects were restricted to spatial memory, with non-cycling females outperforming cycling females independently of age. Unexpectedly, older chimpanzees were better than younger individuals in understanding causality relationships based on sound.

1. Introduction

Cognitive impairment affects a large portion of the older population in the United States. Recent estimates provided by the Aging, Demographics, and Memory Study (ADAMS) indicate that as much as 22% of adults 71 years and older experience cognitive impairment without dementia (Plassman et al., 2008). Annually, about 12% of these individuals progress to dementia. Cognitive impairment, which is associated with decreased quality of life, increased disability, and increased neuropsychiatric disorders, has a great impact on patients, families, and society as a whole. As the number of older persons continues to increase rapidly, there is an urgent need for new interventions to slow or prevent cognitive aging and dementia.

The pattern of aging in human beings is unique among primates in a number of ways. The most obvious of these is that the human is the longest living of all primates, with a maximum lifespan of more than 100 years, nearly double that of our nearest evolutionary relative, the chimpanzee. Another human-exclusive trait is the long period of healthy post-reproductive life of women, in stark contrast to other primates, which usually die before menopause (Walker and Herndon, 2008). Humans are also susceptible to such age-related diseases as Alzheimer's disease and Parkinson's disease, which are absent in all other primates (Finch and Austad, 2012; Heuer et al., 2012). Because this unique human aging phenotype emerged during the 6 million years since the human line diverged from that of the chimpanzee and bonobo, it must result from a relatively small number of genetic changes. In view of these evolutionary changes, we have argued that the pattern of aging in the chimpanzee must be studied to shed light on our own pattern of aging including the neuropathological burdens that accompany it (Herndon and Walker, 2010).

Yet, only 3 studies have examined age-related cognitive decline in chimpanzees (for review, see Lacreuse and Herndon, 2009). Bernstein (1961) studied the rate of learning, memory, and response variability in 8 young (11–19 years) and 8 old (28–40 years) chimpanzees of non-specified sex in object discrimination tasks and a wheel-rotating task. No differences between the age groups were revealed in any of the tasks. Similar results were obtained in another study in 19 chimpanzees of non-specified sex (7–41 years) that were tested on 2 object discrimination tasks (Riopelle and Rogers, 1965). However, poorer performance with age was observed in a version of the Delayed

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Response task, in which the chimpanzees had to remember the location of a reward after various delays. Unexpectedly, compared to young chimpanzees, older chimpanzees were impaired for short delays of 0 or 5 seconds, but not for the longer delay of 10 seconds. A significant decline with age was also found in a 4-choice oddity task, in which chimpanzees were required to select one odd stimulus among 4 stimuli. The third study was an attempt to replicate these findings and revealed no difference in performance as a function of age (Bloomstrand and Maple, 1985). The results from these 3 early studies must be replicated in larger samples, wider age ranges, and broader cognitive domains. Such investigations are pressing, as the permanent funding moratorium on chimpanzee breeding (Cohen, 2007; Knight, 2008), along with the recent implementation of strict limitations on chimpanzee research (Altevogt et al., 2011) will necessarily result in a major decline in laboratory chimpanzee numbers over the next decades. These increased restrictions will not eliminate all chimpanzee research, as some of these studies could be conducted in zoos or sanctuaries (see http://news.sciencemag.org/sciencenow/2013/05/live-chat-should-chimpanzees-be.html for more on this debate).

Recently, a test battery was developed to study physical and social cognition abilities in a variety of primates. The Primate Cognition Test Battery (PCTB) (Herrmann et al., 2007) includes a set of 16 tests that probe Physical and Social Cognition. Physical Cognition included 3 scales of Space, Quantity, and Causality. Social Cognition was subdivided into Social Learning, Communication, and Theory of Mind. We used a modified version of this battery (Russell et al., 2011) to assess cognitive abilities across the chimpanzee lifespan. Our rationale for the use of the PCTB in this study was based on 3 main factors: (1) the PCTB had already been used to effectively compare chimpanzees and humans in a developmental context (Herrmann et al., 2007); (2) the battery included tests of social cognition in addition to tests of physical cognition; and (3) the battery could be easily administered to the apes. Female chimpanzees, of ages representing the entire adult life span, were studied annually for 3 years. We focused on females because they live longer than males (Hill et al., 2001), and because selection related to post-reproductive robustness would be expected to target females more than males (Hawkes et al., 1998, 2011).

When considering female cognitive function, it is essential to examine hormonal status, which may significantly affect performance on selective tasks. Indeed, many studies in women have reported that low estrogen conditions due to surgical (Nappi et al., 1999; Sherwin, 1988), pharmacological (Craig et al., 2008; Sherwin and Tulandi, 1996), or natural menopause (Berent-Spillson et al., 2012) led to impaired performance, most consistently on tasks of verbal memory and verbal fluency. Such hormone-dependent fluctuations in cognitive performance have also been found across the menstrual cycle, with verbal memory being better and spatial ability worse when estrogen levels were elevated, and spatial memory best and verbal memory lowest when estrogen levels were low (Hampson, 1990). Changes in cognition according to the menstrual cycle (Lacreuse et al., 2001), natural menopause (Roberts et al., 1997), or surgical menopause (Lacreuse et al., 2000) have also been observed in female rhesus monkeys. In the present study, we included hormonal status (cycling vs. non-cycling) to examine its possible influence on cognitive performance. Finally, rearing history has been found to greatly influence performance on the PCTB in chimpanzees (Russell et al., 2011), in that extended contact with humans led to better understanding of rotation, quantities, and causal relationships inferred from sound, as well as better understanding of social cues, better production of gestures to a hidden reward, and better modality-appropriate communication. To control for the potential effect of rearing on these tasks, rearing history was included as a factor in the analysis.

2. Methods

2.1. Subjects

Thirty-eight adult female chimpanzees (*Pan troglodytes*) were studied; they ranged in age from 10–54 years (Table 1), covering nearly the entire adult life span. Subjects lived in social groups of 2–6 compatible individuals at the Yerkes National Primate Research Center (YNPRC) of Emory University. Five groups consisted only of females, and 9 groups included a male as part of the social group. The chimpanzees were part of a larger project investigating the effects of aging on cognition and the brain. Because ovarian hormones may influence cognition, the chimpanzees were removed from all forms of hormonal contraception before the onset of the larger project, about 2 years before the present observations began. In addition, anogenital swelling was observed and rated in all chimpanzees 5 days/week. As a part of husbandry practices at YNPRC, some apes were raised in a nursery, rather than by their mothers. In the nursery, human caregivers provide food, sensory stimulation, and play. Of the 38 chimpanzees studied, 18 were nursery reared. For the analyses in this paper, animals were defined as nursery-reared if they entered the nursery within the first 30 days of life.

The chimpanzees were humanely treated in accordance with the Animal Welfare Act and the US Department of Health and Human Services "Guide for the Care and Use of Laboratory Animals." All research reported in this manuscript complied with the protocols approved by the Animal Care and Use Committee of Emory University. The YNPRC is accredited by the Association for Assessment and Accreditation of Laboratory Animal Care International.

2.2. Hormonal status

Ovarian cycles can be tracked in chimpanzees by observing and rating anogenital swelling. Swelling was rated on a 5-point scale, and menstrual bleeding was recorded if observed. This procedure reliably indicates the occurrence of ovulation (Graham, 1979; Lacreuse et al., 2008), as recently confirmed by urinary hormone levels in a subset of the chimpanzees used in this study (Herndon et al., 2012). These observations allowed us to separate chimpanzees into those who were cycling normally and those who were not (Table 1). Cycling and non-cycling chimpanzees were present in all age groups. The presence of cycling in aged chimpanzees and its absence in some young and middle-aged chimpanzees is discussed elsewhere (Herndon et al., 2012; Lacreuse et al., 2008).

2.3. Cognitive and motor testing

We used a modified version of the Primate Cognitive Testing Battery (PCTB), which was designed by Herrmann et al. (2007) to

Table 1
Number of female chimpanzees studied in each age group, with and without menstrual cycles

	Young	Middle-aged	Old	Oldest-old	Total
	10–16 y	17–29 y	30–49 y	50–54 y	
With menstrual cycles	6	9	8	1	24
Without menstrual cycles	6	4	1	3	14
Total	12	13	9	4	38