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Effects of aging and hormonal status on bimanual motor coordination in the rhesus monkey

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Abstract

Studies of age-related changes in motor function in nonhuman primates have been based exclusively on unimanual motor tasks. In this study, we examined whether aging affects bimanual motor coordination in the monkey model. In addition, we compared performance of ovariectomized and intact females on the task, to examine whether estrogen deficiency impairs motor function. The task required 29 rhesus monkeys (6–26 years old) to extract a maximum of 15 raisins from a testing hole-board. While the task could most efficiently be performed with two hands, other motor strategies were possible. The number of raisins extracted per minute was measured in each of eight sessions, the first and last of which were videotaped for analysis of motor patterns.

The number of raisins retrieved per minute declined significantly with age. All monkeys improved with practice, but aged monkeys improved more slowly than young ones. The proportion of bimanual actions tended to increase between the first and the last sessions but was not significantly different between young and aged monkeys. Hormonal status did not affect performance. Finally, performance on the bimanual task was significantly correlated with performance on a previously administered unimanual motor test emphasizing speed, suggesting that age-related motor slowing may explain deficits in both tasks.

Keywords: Estrogen; Handedness; Macaque; Manual strategies; Ovariectomy

1. Introduction

The progressive deterioration of motor function is a universal feature of aging [3,22,25]. Age-related decline of manual activity is apparent in manual dexterity [8,19,25], manual speed [3,22,25], grip strength [11,22,27], pinch strength [22], tactile sensitivity [4,15,22] and motor coordination [21,28,33,34].

Age-related motor dysfunction is thought to reflect underlying age-related degeneration of the nigrostriatal dopaminergic system [6]. In particular, decreases in the number of tyrosine hydroxylase and dopamine transporter immunoreactive cells in the substantia nigra [7], decreases in nigrostriatal dopamine levels [12], declines in dopamine D2 receptor binding [31] and reductions in dopamine release in the substantia nigra and putamen [9] have been shown to be associated with age-related motor decline in primates. Conversely, the chronic infusion of a dopaminergic trophic factor (GDNF) into the lateral ventricles improves motor function in aged monkeys [10].

Estrogens modulate the activity of striatal dopamine cells and dopamine-mediated behaviors, such as sexual behaviors in the female rats [2,14]. In addition, estrogen treatment in ovariectomized (OVX) animals has been shown to restore striatal dopamine release in rats [20] and the number of dopaminergic cells in the substantia nigra in vervet monkeys [18]. Estrogen use was associated with improvements of parkinsonian symptoms in one study in old women [24] and the addition of estrogen therapy to existing antiparkinsonian

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medication for 8 weeks improved motor dysfunction in women suffering from Parkinson's disease (PD) with motor fluctuations in another study [30]. Furthermore, estrogen has been shown to improve motor function in young women across the menstrual cycle [13] and in girls suffering from Turner's syndrome [23]. These findings suggest that estrogens may protect the dopaminergic system and preserve or improve motor function in young and elderly subjects. However, other studies have failed to find an effect of estrogen replacement on motor function. For example, gross motor functioning remained unchanged after estrogen replacement in a placebo-controlled study in women with PD [29]. Likewise, we failed to find changes in fine motor function following estrogen replacement in a recent study in young and aged OVX female rhesus monkeys [17].

The rhesus monkey is an excellent model of human age-related motor impairments [35]. However, the similarities between human and monkey age-related fine motor deficits have been based on tests of unimanual motor function, such as the lifesaver task, which requires monkeys to remove a lifesaver candy from wires of different complexity [35]. Other unimanual motor tests, such as the rosette and cap tests used by Bachevalier et al. [1] have failed to show age-related changes in monkeys. Bimanual motor coordination, however, is essential to human activities, as the majority of everyday movements require some degree of collaboration between the hands. Given this complexity of human manual activities, it is clear that additional motor abilities need to be investigated in the monkey model. A few studies have shown that bimanual coordination declines with age in humans [28,33,34], but age-related effects on bimanual motor function have not been investigated in nonhuman primates.

In the present study, we examined the effect of age on performance of a bimanual task, a task designed to be most efficiently performed with two hands. In addition, we compared performance of ovariectomized females with that of gonadally intact females on this task. Finally, we examined the relationships between bimanual coordination performance and unimanual performance in the lifesaver task in a subset of eight gonadally intact monkeys who performed both tasks.

2. Methods

2.1. Subjects

We studied 29 rhesus monkeys (*Macaca mulatta*), aged 6–26 years old, including 26 females (21 intact, 5 OVX) and 3 males (Table 1). The OVX females had been without ovaries

Table 1
Monkeys code, age in years, sex, and hormonal status (INT = with intact ovaries or testes; OVX = ovariectomized) are given in columns 1–4

Monkey code	Age	Sex	Hormonal status	Mean number of raisins (out of 15)	Mean latencies (*s*) (max = 180)	Mean number of raisins/minute
RLf7	6.07	F	INT	13.75	75.50	14.05
Ph1019	6.08	F	INT	14.88	72.13	14.99
RDc7	6.14	F	INT	14.50	46.13	20.64
RR6	7.07	F	INT	14.38	66.50	18.46
RVo6	7.14	F	INT	14	113.63	9.81
RZm6	7.18	F	INT	14.25	53.25	18.12
RYi6	7.28	F	INT	10.75	57.25	16.52
RLc6	8.14	F	INT	9.75	161.38	3.99
RTb6*	8.16	F	INT	14.75	73.81	14.98
RSt5	9.09	F	INT	14.63	81	12.93
REj5*	10.09	F	INT	13.25	132.13	7.05
RRd5	10.2	F	INT	13.63	57	16.02
RMo4*	11.78	F	INT	12.63	114.50	8.55
RDf4*	12.16	F	INT	13.25	118.63	7.31
RGc4*	12.25	F	INT	13.88	89.38	10.07
RWv3	13.13	F	INT	1.75	180	.58
RCe3*	14.26	F	INT	14.50	101.25	9.06
RQy2	15.15	F	INT	11.17	148	2.74
REv2	15.2	F	INT	6.63	180	2.20
RJw1	18.09	F	INT	8.38	180	2.79
Nm5	9.89	F	OVX	8.38	162.75	3.48
Pu4	11.15	F	OVX	13	119.50	8.53
Jg4	12.14	F	OVX	11.63	154.88	5.24
Ld4	12.19	F	OVX	14.38	74.13	13.32
Fr3	13.21	F	OVX	14.25	96.88	10.51
Er	26.05	F	OVX	6.38	180	1.96
I679*	21.14	M	INT	7.88	180	2.62
E313*	21.16	M	INT	10.50	161.50	4.35
H918	21.72	M	INT	14.38	98.88	9.32

Also given (columns 5 and 6) are the mean number of raisins successfully removed and the mean latency in seconds to remove the raisins in the eight sessions. Column 7 shows the mean of the rates of removal of the raisins (raisins/min) for the eight sessions.
* indicates intact monkeys also tested on the Lifesaver task.