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Effects of constant daylight exposure during early development on marmoset psychosocial behavior

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A B S T R A C T

Due to global industrialization, the light cycle is shifting to longer daytime. Mounting evidence indicates that social developmental disorders may correlate with longer periods of daytime in childhood. However, the exact mechanisms of this link remain unclear. To examine the impact of longer day-time on psychosocial development, we developed a novel non-human primate model, using the common marmoset (*Callithrix jacchus*) reared under constant daylight from birth. Marmosets were reared individually by human nursing under constant light (LL) during varying periods in juvenile development, and their behaviors were compared with those of normal day–night cycle (LD) marmosets by multivariate analysis based on principal component analysis (PCA). LL marmosets elicited egg-like calls (e-call) less in juvenile period, and displayed side-to-side shakes of the upper body with rapid head rotation through adulthood frequently. Based on the PCA, these behaviors were interpreted as 'alert' or 'hyperactive' states. Additionally, behavioral development of marmosets reared under constant dark (DD) was markedly different from both LD and LL marmosets, suggesting the fundamental importance of daylight-dependent neuronal and endocrine processes and entrainment by a constant 24-hour light/dark cycle on psychosocial behavior development.

1. Introduction

Disturbances of circadian rhythm due to abnormal lighting conditions may be involved in the pathogenesis of various psychiatric disorders, such as insomnia, depression, and mental maldevelopment (Germain and Kupfer, 2008; Kohyama, 2009; Lewy, 2007), presumably through neuronal and hormonal mechanisms regulating sleep, temperature, and mood cycles (Bunney and Potkin, 2008). Animal research has confirmed the importance of circadian rhythms for hormonal and behavioral functioning (Cambras et al., 1998; Connolly et al., 1983; Diez-Noguera and Cambras, 1990; Mistlberger and Skene, 2004; Schelstraete et al., 1992; Toki et al., 2007; Yerushalmi et al., 2006). Recent animal studies examined the development of circadian rhythm itself, as well as the relationship between circadian rhythm and socio-emotional behavior in two ways: the effect of social zeitgeber (time-cue) on circadian timing, and the effect of circadian rhythm on socio-emotional behavior (Mistlberger and Skene, 2004; Toki et al., 2007). However, the direct effect of abnormal circadian rhythms in early life on social behavior development is difficult to study due to the tight mother–infant interaction in mammalian models (Schelstraete et al., 1992; Toki et al., 2007). To examine the impact of longer day-time on psychosocial development, we have developed a novel common marmoset (*Callithrix jacchus*) model in which the subjects were fed milk by humans until weaning, and then isolated from other marmosets to simplify the social experience. In this experimental setup, we were able to examine directly the effects of early atypical light zeitgeber on psychological behavior in social contexts. Furthermore, we have developed a new approach to quantify and detect the subtle differences of complex psychological behaviors using a multi-parametric visualization of social interaction based on principal component analysis (we named as 'Bouquet analysis').

In this study, subjects were raised individually by human nursing for several months from birth under either normal (12 h light:12 h dark cycle; LD) or constant light (LL) conditions, or as another extreme condition, constant dark (DD). From the video recordings over the developmental time period (postnatal days 30–440), behavior parameters were extracted and assessed by principal component analysis (PCA). We found that LL group had subtle but important features in the

Abbreviations: PCA, principal component analysis; LD, 12 h light and 12 h dark cycle condition; LL, constant 24 h light condition.

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one call type associated with seeking alert that could be visualized as a unique developmental pattern in each group through adolescence and adulthood. These results suggest that circadian rhythms in early life affect psychosocial development persisting through adulthood.

2. Methods

2.1. Animals

The experimental protocols were approved by the Animal Care and Use Committee of the Tokyo Metropolitan Institute for Neuroscience. Immediately after birth, marmoset babies were isolated from their parents, and were fed on milk until weaning. They were housed individually in transparent plastic cages (22 × 14 × 14 cm) with paper sheets on the cage floor. Each cage was placed in a light-sealed incubator illuminated by a fluorescent lamp maintaining constant temperature (32 °C). Approximately 25 days after birth, each animal was transferred into a stainless-steel grid cage (40 × 27 × 22 cm), and then put into a larger cage (40 × 37 × 53 cm) afterward. After weaning, conventional chow and water were given ad libitum throughout the remainder of the experiment (total 24 marmosets).

To examine effects of photic environment during early life on behavioral development, the marmoset babies were raised under one of three lighting conditions: (a) 12 h light (L) and 12 h dark (D) cycle (LD) as normal control, (b) constant light (LL), or (c) constant dark (DD) (see Fig. 1d). Light intensity per cage was 750–930 lx during the light period, and 0 lx in the dark period of LD and DD. For developmental trajectory analysis, we set three age steps to test the behavioral battery, (I) postnatal day 0-99 (P0-99d), (II) P100-269d, and (III) P270-440d. Each subject experienced various lengths of LL and LD periods as shown in Fig. 1d with each subject number at Fig. 1e and averaged age at Fig. 1f.

2.2. Development of marmoset circadian rhythm monitored by locomotive activity

Locomotor activity of the 7 marmosets was monitored continuously from birth to P120d with an infrared detecting device (NS-AS01;

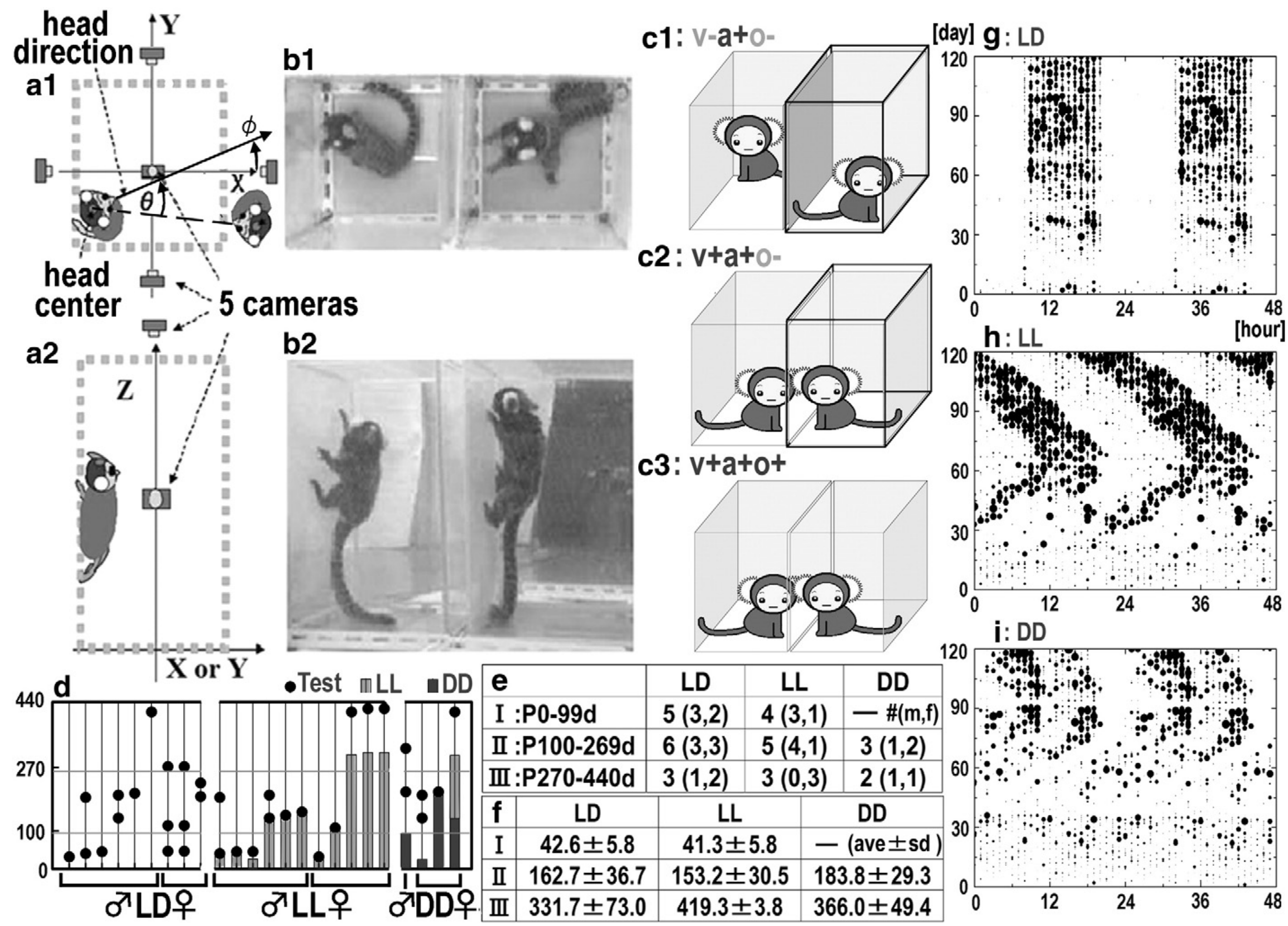

Fig. 1. Experimental conditions and locomotor activity patterns of LD, LL and DD animals from the birth to 4 months. a1–2. The behavioral test scheme of the top (a1) and side (a2) view with the position of five videocameras and several behavioral parameters for quantification, head center movement direction, and head-nose direction angles, i.e., absolute angle (phi) or relative to others (theta). b1-2. Photos of a behavioral test from top- or side-view. c1-3. Contextual procedures considering social interaction through stepwise combination of different sensory modalities (v; visual, a; auditory, o; olfaction). The mutual interaction of two subjects in each behavior test box was video recorded. d. The photic cyclic regulation of each subject under LD, LL and DD condition and the days of behavior test were indicated by closed circle. The photic conditions until the day of behavior test were indicated by bar (LL: gray, DD: black). The period under LD condition was without bar. e–f. Summary of experimental subjects. e. The number of subjects under each lighting condition at each age-stage. f. Each averaged age with the standard deviation summary. g–i. The activity was monitored by the infrared-based recorder and represented as a raster plot. g: A typical pattern of the activity rhythm development in a LD subject. In the first 23 days of this example, there was an arrhythmic period. After this period, the circadian rhythm was entrained by light. h: The activity rhythm development in a LL subject. The arrhythmic period was 44 days in this case, but no light-entrainment was established beyond this period. The free run rhythms changed from longer than 24 h to shorter around P80d. i. An example of a DD subject's pattern. Although free-run was confirmed, its cycle seemed to be ambiguous compared to LL.