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Review article

Susceptible period of socio-emotional development affected by constant exposure to daylight

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ABSTRACT

As a diurnal experimental primate, the common marmoset (*Callithrix jacchus*) has recently contributed to numerous kinds of studies of neurobiological psychiatry as an essential pre-clinical model. The marmoset matures sexually within one or two years after birth. Thus, we can observe how the primate learns and develops psycho-cognitive functions through experiences in experimental environment for a much shorter period compared to that of humans.

Longer daylight exposure may affect psychological development of children. In our research, we focus on raising marmosets under constant daylight from birth until various ages. In order to quantitatively evaluate the development of higher-ordered psychological functions, we designed a system of socio-behavioral tests and multivariate correlation analysis methods based on principal component analysis. With reference to the call and typical body movement expressed during a particular social context, we statistically inferred the emotional features of the subjects.

In the current literature, we review our published results showing increased alert behaviors by constant light, and then, attempted to extend our additional analysis to seek age-dependent susceptibility to constant light. We then present the neurobiological mechanisms with reference to previous research reports. The current review suggests possible existence of a susceptible period earlier than three to five month-old in the environment-induced developmental disorder model, supposedly like attention deficit hyperactive disorders (ADHD) or oppositional defiant disorder (ODD).

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Abbreviations: AChE, acetylcholine esterase; ADHD, attention deficit hyperactive disorders; ASD, autistic spectrum disorders; ODD, oppositional defiant disorder; ChAT, choline acetyltransferase; DAT, dopamine transporter; DD, constant dark; DIA, dehydroascorbic acid; DTA, diphteria toxin α subunit gene; ipRGC, intrinsically photosensitive retinal ganglion cells; GSH, glutathione; LD, light–dark cycle per 12 h; LHb, lateral habenula; LL, constant light; mAmy, medial amygdala; NOS, nitric oxide synthase; PCA, principal component analysis; SCN, suprachiasmatic nuclei; SERT, serotonin transporter; sPVZ, subparaventricular nucleus; VLPO, ventrolateral preoptic area.

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1. Introduction

In etiological consideration of mental disorders, we need to study developmental processes of the neuronal circuit formation in early life. The typical psychological development of children is thought to occur progressively through diversification of the neuronal circuit by interaction between their own biological bases and surrounding environment. In childhood, our sensitivity to the environment seems higher and the response is simpler like examples of primitive reflexes that are transiently appeared and disappeared in neonates. Emotional behaviors such as 'crying' seem to be more easily triggered by physiological conditions in preschool-age children. Acute and chronic environmental stimuli in early life must crucially affect the neuronal circuit development of psychological function leading to form future higher-order circuitry responsible for more complex mental processing.

If the initial development is suppressed by deficiency in genetics of the biological basis and in the environmental factors, it may cause susceptibility to social stress in a later developmental stage and complex co-morbidities of mental disorders like attention deficit hyperactive disorders (ADHD), autism spectrum disorders (ASD), oppositional defiant disorder (ODD), or schizophrenia.

Among the many critical environmental factors for socio-emotional development after birth, we focused on light-induced circadian rhythm (Senoo et al., 2011). It is a common key factor which includes the sleep–awake cycle and its disturbance as seen in various psychiatric disorders. We selected a common marmoset (*Callithrix jacchus*) as the primate model of the study due to its particularly superior psychological function such as cooperative communication (Flack, 2013) and altruisms (Burkart et al., 2007), which is supposedly affected by its environment within one year from birth to early adulthood, as well as its rich socio-communicative behaviors. Such behaviors include multiple kinds of calls, emotional and social approaching or discrimination of typical motion (Pistorio et al., 2006; Yamaguchi et al., 2010; Senoo et al., 2011; Koshiba et al., 2011, 2013a; Cross and Rogers, 2004).

Another important consideration of the study on an animal model is the quantitative and objective methods to evaluate the socio-emotional behavior and higher-order psychological states in developing common marmosets from neonate to adulthood (Koshiba et al., 2011, 2013a). As a basic approach, we used multi-dimensional correlation analysis, mainly, the principal component analysis (PCA) and time-series regression analysis. The neuronal networks of higher ordered psychological function is supposedly re-wired one another by multiple domains of different functions formed in different stages during development. The complex networks may be able to be estimated mathematically with quantitative information processing by such multivariate analyses. In our previous studies, the complex functional domain correlation was visualized by multivariate analysis using multiple but extracted simple factors in behaviors, biological molecules and physiological information. We call the method as 'Behavior Output Analysis for Quantitative Emotional State Translation (BOUQUET)' which allows us to hypothetically visualize 'higher-order neuro-psychological modulation'. The BOUQUET method has been repeatedly used to evaluate common marmosets and also human groups with ASD and their typical developing siblings. We further used the BOUQUET method to analyze environment-induced developmental disorder models in domestic chicks. Their social acute and chronic experience were tested on visual, auditory, tactile and olfactory perception of peers and parents (Koshiba et al., 2011, 2013a,b,c,d,e; Mimura et al., 2013a,b,c; Shirakawa et al., 2013a,b).

In the current review, we referenced our previous report with regards to the developmental socio-psychology under 'environmental constant light' in common marmosets (Senoo et al., 2011). This study was motivated by a recent social issue of longer light exposure especially on preschool-age children that is well-known about the sensitive age-stage for multiple kinds of learnings (Ito, 2004). In this report we analyzed twenty-five parameters derived from the behavioral data taken from videos of twenty-four common marmosets from birth to adult. We summarized that the primates exposed by constant light during early development had typical alert body-motion and more calling behaviors at meeting contexts with unfamiliar peers. The behavioral types of active and alert emotion might be interpreted as models of ADHD or ODD either of which is diagnosed with irritable phenotypes by DSM-IV (Drabick and Gadow, 2012). Alert emotion is rather categorized in lower-ordered function that may be internalized in adults to avoid careless expression in social contexts. The LD subjects, supposedly regarded as the control group comparing to LL seemed to express their higher-ordered function as suppression of the lower-ordered functions at peer-social contexts in adult more clearly than in juvenile. The behavioral developing pattern that could be visualized in the multivariate correlation structure by BOUQUET might be interpreted one model of developmental disabilities of peer-social adjustment in LL group. In this review, we, furthermore, added new analyses of the same data to consider any susceptible period of more specific age to form the character to express rather emotionally negative behavior, supposedly caused by neuro-psychological network formation of social emotion in limbic systems (Amaral et al., 2008; Machado and Bachevalier, 2003; Lesch and Waider, 2012; Happé and Frith, 2014; Leppänen and Nelson, 2009). Finally, according to the relevant reports in developmental psychiatry, the three key terms are, susceptible period learning, circadian rhythmicity, and expected supporting tools for treatment.

2. Effects of constant light during early life to socio-psychological behavior development and susceptibility to earlier arrhythmic periods of locomotion and sensory context dependent on socio-behavioral modulation around weaning age

In common marmoset (*Callithrix jacchus*), we developed socio-psychological developmental model and multi-dimensional analysis which we call BOUQUET, to imply complex neuro-psycho-cognitive mechanisms generally (Koshiba et al., 2011). We applied it to examine the impact of longer exposure to daylight in early life (Senoo et al., 2011). The subjects were fed milk by humans until weaning (Tokuno et al., 2012) and were isolated from any other marmosets from birth until adult age. We simplified the

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