

Spindle Evolution in Normal and Mentally Retarded Children: A Review

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Summary: In neonates and infants, sleep-wake parameters indicate characteristic ontogenetic features. Sleep spindle activity also changes with maturation in terms of frequency, amplitude, and amount. For this reason, spindles are one of the useful indices of cerebral function in infants. The literature on the development of spindles in normal and mentally retarded children is reviewed. **Key Words:** Spindle evolution—Normal children—Mentally retarded children—Spindle disorders.

A characteristic electroencephalogram (EEG) feature of light sleep in infants is the presence of sleep spindles. Spindles are best seen in the parietal and frontal cortices; the duration of each spindle burst varies from 1 to 3 sec; the frequency varies between 14 and 10 Hz and tends to be lower in older children; the voltage varies from 30 to 50 μ V and tends to be higher in older children. As for the ontogenesis of spindles, they are already seen in neonates (Petre-Quadens, 1966; Roffwarg et al., 1966; Hagne, 1972; Metcalf and Jordan, 1972). This spindle activity, however, disappears with increasing age and reappears during non-rapid eye movement (NREM) sleep by 3 months of age, when it shows features similar to those encountered in adults (Schultz et al., 1968; Lenard, 1970; Metcalf and Jordan, 1972; Schulte and Bell, 1973; Tanguay et al., 1975; Gibbs and Gibbs, 1978). Spindle activity also varies with maturation in terms of frequency, amplitude, amount, and location.

Ontogenesis of Sleep Spindles in Normal Children

From Birth to 3 Months

In normal full-term newborns, low-voltage (Petre-Quadens, 1974) and poorly defined (Hagne, 1972; Metcalf and Jordan, 1972) vertex sleep spindles lacking the

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typical spindle form and duration (Roffwarg et al., 1966) are observed. As for the developmental course of spindles in full-term infants (Metcalf and Jordan, 1972), the "rudimentary" prespindle lasts a few days, followed by poorly developed Grade I spindles persisting for approximately 7–10 days after birth; these give way to well-developed Grade II spindles. Grades I and II spindles were defined by Metcalf (1970) as follows: Grade I spindles are localized in the vertex, are not fusiform in modulation, and are 0.4–1.0 sec in duration with an amplitude of 7–10 μV ; Grade II spindles are vertex-dominant but may occur simultaneously in anterior regions, are fusiform, and are 1–3 sec in duration with an amplitude of 25–30 μV . Well-defined spindles begin to make their appearance between 4 and 9 weeks (Samson-Dollfus et al., 1964; Paul et al., 1973; Dreyfus-Brisac, 1979; Ellingson and Peters, 1980a) and emerge only during high-voltage slow wave sleep. Spindle bursts seldom are seen before 4 weeks of age and may not develop before 7 or 8 weeks on rare occasions. When premature infants are compared to full-term infants (conceptional age), the earlier onset of spindles in the former (Ellingson and Peters, 1980b) suggests that the relevant central nervous system is particularly susceptible to the influence of environmental factors. If the curve for the incidence of spindles among premature infants of different ages from birth to 11 months is compared with a similar curve for normal control subjects, the two groups are seen to differ not only in the age at which spindles appear (as might be expected, spindles appear later in premature than in full-term infants), but also in the incidence of spindles, which remains lower at all ages among premature than among full-term infants (Gibbs and Gibbs, 1978).

Preterm infants show somewhat different types of spindle-like activity in both REM and NREM sleep (Parmelee et al., 1968b; Watanabe and Iwase, 1972; Lombroso, 1979). According to Parmelee et al. (1968b), this EEG activity in the frequency range of sleep spindles occurs during REM sleep in both pre- and full-term neonates but disappears in the 3-month-old baby. Watanabe and Iwase (1972) report that spindle-like fast rhythms occur in the central and occipital areas during all behavioral states in low-birthweight infants (preterm and small-for-dates) but disappear completely around term.

From 3 Months to 5 Years

By 3 months of age, mature sleep spindle bursts are present almost invariably during NREM sleep and are similar to those seen in adults. Figure 1 shows spindles recorded from Fp1-T3, Fp2-T4 leads during stage 2 sleep at 4, 7, 61, and 68 months in normal children. Spindle activity increases, reaching a peak between 3 and 9 months (Fois, 1961; Schultz et al., 1968; Lenard, 1970; Metcalf and Jordan, 1972; Schulte and Bell, 1973; Tanguay et al., 1975; Gibbs and Gibbs, 1978; Sterman, 1979). During the second year of life, spindle activity decreases, reaching a minimal level at 27 months (Gross and Schulte, 1969; Lenard, 1970; Tanguay et al., 1975), remains fairly constant to 54 months, then rises to the level of older children (Tanguay et al., 1975) (Table 1). Metcalf and Jordan (1972), on the other hand, have argued that there is in fact an increase in short spindles (about 1 sec in duration) during the second year of life and that by 18 months of age there may be as many as 4–5 spindles/10 sec of EEG.

Between right and left hemispheres, sleep spindles have been shown to be

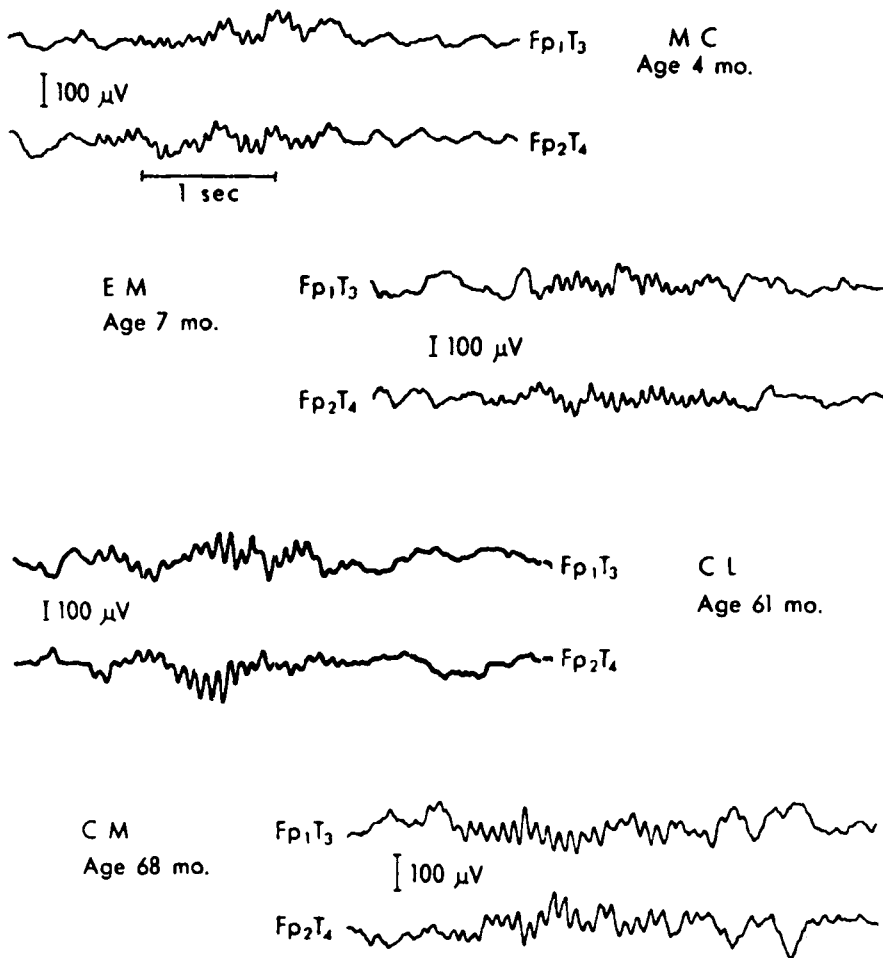


FIG. 1. Sleep spindles recorded from Fp1-T3 and Fp2-T4 leads during stage 2 sleep at 4, 7, 61, and 68 months of age in normal children. Figure 1 is reproduced, with permission of the publisher, from Tanguay et al., 1975.

TABLE 1. Sleep spindle activity during stage 2 sleep measured from Fp1-T3 leads in normal children

Mean values	Age group (months)							
	4-7 (3)	8-18 (3)	19-40 (6)	41-54 (8)	55-68 (6)			
Spindle time during stage 2 sleep (%)	14.0	— ^a —	5.6	— ^a —	0.5	0.7	— ^a —	4.0
Number of spindles/10 sec stage 2 sleep	0.993	0.662	— ^a —	0.078	0.086	— ^b —	0.507	
Spindle-burst length (sec)	1.64	— ^a —	0.95	— ^a —	0.61	0.60	— ^b —	0.78

Numbers of subjects are given in parentheses. Tables 1-5 are adapted, with permission of the publisher, from Tanguay et al., 1975.

^a $p < 0.01$; ^b $p < 0.05$; ^c $p < 0.10$.

asynchronous in the first 3 months (Gibbs and Gibbs, 1978; Ellingson and Peters, 1980a), at months 6–8 (Lairy, 1975), and during the first year of life (Fois, 1961; Hagne, 1972); they also have been shown to be synchronous at months 10–12 (Gibbs and Gibbs, 1978; Ellingson and Peters, 1980c) and at 2 years of age (Dreyfus-Brisac, 1979). Spindle onsets in the right and left sides of the head are more often concurrent in older (> 54 months) as compared to younger (< 22 months) children (Tanguay et al., 1975).

The spindle-wave frequency is 13–14 Hz in children younger than 40 months but is 12–13 Hz in older children (Tanguay et al., 1975) (Fig. 2). The 14-Hz vertex-dominant spindle is commonly observed in children younger than 4 years, while the 12-Hz frontal-dominant spindle is seen in children 4 years or older (Niedermeyer and Capute, 1967).

The voltage of sleep spindles tends to vary with age, being higher in relatively older children (Fois, 1961; Petre-Quadens, 1974). Spindle bursts may reach very high voltage during the second 6 months postterm (Ellingson, 1967).

At 6 Years or Older

As for sleep spindle activity in children of 6 years or older, Fois (1961) reported that the spindles vary somewhat with the depth of sleep, being slower as sleep

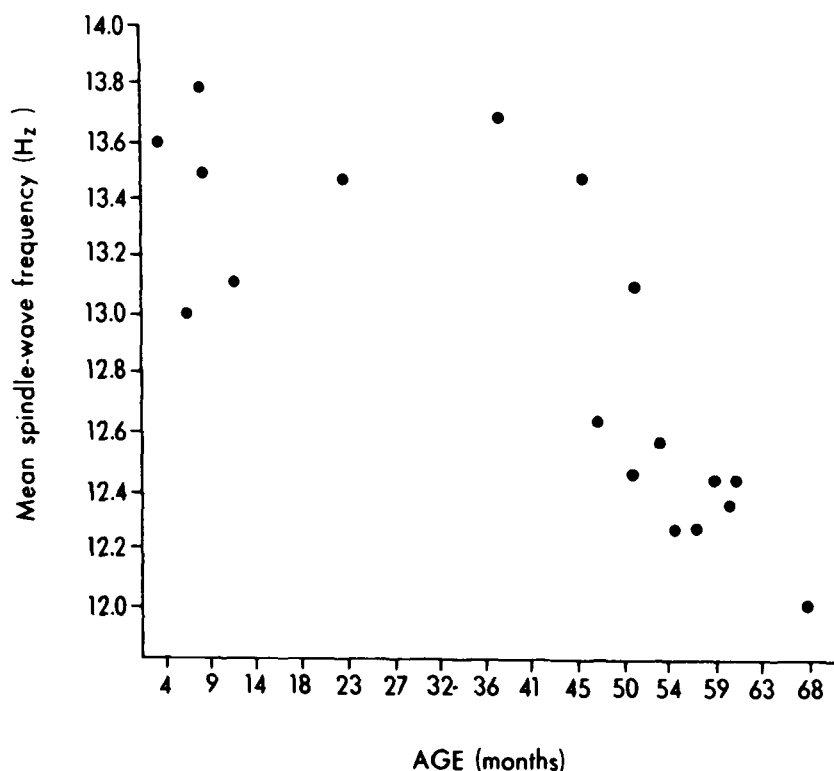


FIG. 2. Mean spindle-wave frequency as a function of age in normal children. Figure 2 is reproduced, with permission of the publisher, from Tanguay et al., 1975.

deepens. In 6- to 7-year-olds, spindles are of higher voltage, occur early in the night, and have a frequency of 13–15 Hz with parietal-occipital predominance. Later in the night, spindles may slow to 9–10 Hz, mainly in the frontal area. In 8- to 14-year-olds, spindles are of lower voltage; 12-Hz spindles occur in somewhat deeper sleep and are more pronounced in the frontal leads.

Development and Disorders of Sleep Spindles in Mentally Retarded Children

Absence of sleep spindles is more commonly observed in mentally retarded than in normal children (Fois, 1963; Gibbs and Gibbs, 1964; Monod and Ducas, 1968; Rhode et al., 1969; Petre-Quadens, 1972; Shibagaki et al., 1980). In particular, the absence of spindles during sleep seen in infants between 3 and 8 months of age is a severe anomaly never seen in normals (Monod and Ducas, 1968; Lairy, 1975).

Extreme spindles are reportedly common in mentally retarded children (Gibbs and Gibbs, 1973) but rare in adult mental retardates (Gibbs and Gibbs, 1964). Extreme spindles are rather similar to normal sleep spindles except for their diffuseness, much higher voltage (200–400 μ V), and more or less continuous nature; they do not correlate with epilepsy but with mental retardation. Cerebral palsy is common (26%) among children with extreme spindles, and the extrapyramidal forms of cerebral palsy are more commonly associated with extreme spindles than are the spastic types (Gibbs and Gibbs, 1964). Moreover, spindle activity increases in children with phenylketonuria (PKU) (Schulte et al., 1973). As there is a report suggesting that mental retardates can have either large amounts of spindle activity or virtually none (Bixler and Rhodes, 1968), no final conclusions about the spindle activity of mentally retarded children can yet be made.

Parmelee et al. (1968a) carried out a longitudinal study of the EEG in abnormal infants. Two mongoloid infants showed normal sleep spindles during quiet sleep at the age of 3 months. However, in two infants with prenatal or perinatal anoxia, spindles during quiet sleep had not developed by 3 or 8 months of age, and these infants later were found to have spastic quadriplegia and mental retardation. Moreover, four hypothyroid infants did not have spindles during quiet sleep until they received thyroid hormone therapy. Schultz et al. (1968), and Lenard and Schulte (1974) also reported that hypothyroid infants showed a diminished number, or total absence, of spindles. After thyroid therapy, some infants developed normal amounts of spindles, but others continued to show deficits. Those infants who developed normal spindle activity tended to demonstrate normal developmental quotients (DQ) on follow-up evaluation, whereas those who did not showed low DQs. In contrast, the number of spindles increased in infants and children with PKU compared to age-matched normal controls (Lenard and Schulte, 1974). Treatment with a low phenylalanine diet did not normalize the number of spindles.

A more recent study by Ellingson and Peters (1980c) has indicated that sleep spindle bursts during slow wave sleep appeared later and were less abundant in a trisomy-21 group than in a control group throughout the first year, and interhemispheric synchrony in the former did not improve significantly by 12 months of age.

TABLE 2. Comparison of developmental quotient in mentally retarded children with and without spindle activity

Spindles	Developmental quotient				
	Neonate	1 year	2 years	3-8 years	Total
Absent	26.2 ± 10.4 (5)	37.8 ± 12.2 (4)	35.3 ± 21.7 (4)	12.4 ± 5.6 (5)	26.8 ± 16.2 (18) ^a
Present	37.2 ± 17.7 (9)	45.1 ± 13.2 (8)	41.0 ± 8.4 (5)	29.3 ± 24.7 (3)	39.6 ± 16.7 (25)

Means ± SD are shown for the numbers of subjects given in parentheses.

^a $p < 0.05$.

We (Shibagaki et al., 1979, 1980) investigated, according to the criteria of Tanguay et al. (1975), the evolution of sleep spindle activity during stage 2 of nocturnal sleep in 43 mentally retarded children aged 4 months to 8 years. The mean ± SD of DQs was 34.3 ± 17.8 . All subjects were inpatients classified into four age groups: 4-11 months ($n = 14$), 1-2 years ($n = 12$), 2-3 years ($n = 9$), and 3-8 years ($n = 8$). Only one infant had extreme spindles. A low DQ tendency was observed in infants without spindles as compared to those with spindles in all age groups (Table 2). Figure 3 shows spindles recorded from F3-C3 and F4-C4 leads during stage 2 sleep, with examples from each of the four age groups. No significant differences were found among the age groups in mean percent spindle time during stage 2 sleep, mean number of spindles per 10-sec stage 2 sleep, mean spindle-burst length, and mean spindle-wave amplitude (Tables 3 and 4). A significant decrease in mean spindle-wave frequency was found in 4- to 6-year-olds as compared with the 4-11 month-, 1-year-, and 2-year-old groups (Table 4, Fig. 4). This tendency is similar to that found in normal children (Fig. 2). When our cases were rearranged into the four age groups used by Tanguay et al. (1975), i.e., 4-7, 8-18, 19-40, and 55-68 months, no differences in spindle activity were found

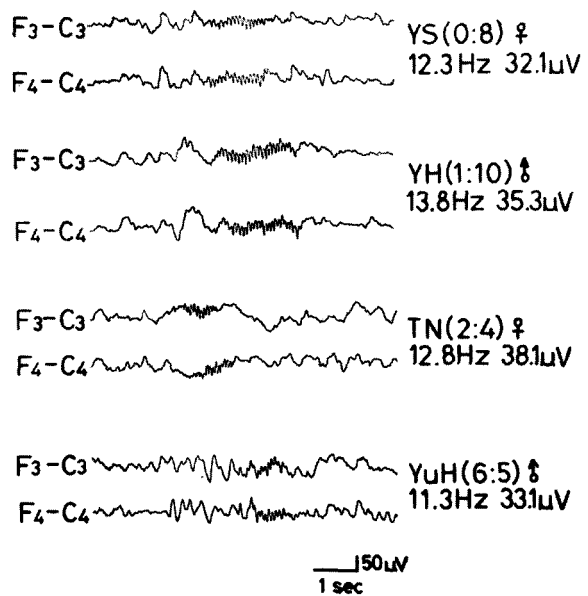


FIG. 3. Sleep spindles recorded from F3-C3 and F4-C4 leads during stage 2 sleep in mentally retarded children. Examples of four different age groups are given.

TABLE 3. Comparison of mean spindle time during stage 2 sleep and mean number of spindles/10 sec stage 2 sleep in four different age groups of mentally retarded children

Parameter	Age group				Analysis of variance
	Neonate	1 year	2 years	3-8 years	
Spindle time in stage 2 (%)					
A	1.4 ± 1.2 (13)	2.0 ± 2.5 (9)	0.9 ± 1.3 (8)	1.1 ± 1.6 (8)	ns
B	2.2 ± 0.6 (8)	3.6 ± 2.3 (5)	1.8 ± 1.2 (4)	3.1 ± 0.9 (3)	ns
Number of spindles/10 sec stage 2					
A	0.144 ± 0.131 (13)	0.218 ± 0.225 (9)	0.103 ± 0.138 (8)	0.130 ± 0.178 (8)	ns
B	0.235 ± 0.082 (8)	0.393 ± 0.152 (5)	0.206 ± 0.130 (4)	0.346 ± 0.098 (3)	ns

Means ± SD are shown for the numbers of subjects given in parentheses. Sampling was done from the F3-C3 leads. A, subjects with and without spindle activity; B, subjects with spindle activity.

TABLE 4. Comparison of mean spindle parameters in four different age groups of mentally retarded children

Parameter	Age group				Analysis of variance
	Neonate (8)	1 year (5)	2 years (4)	4-6 years (3)	
Spindle-burst length (sec)	1.02 ± 0.19	0.93 ± 0.20	0.76 ± 0.09	1.00 ± 0.07	ns
Spindle-wave frequency (Hz)	13.9 ± 1.5	14.2 ± 0.7	13.5 ± 1.1	11.2 ± 0.5	$p < 0.05$
Spindle amplitude (μ V)	47.9 ± 18.5	44.3 ± 7.0	37.6 ± 10.1	63.5 ± 29.1	ns

Means ± SD are shown for the number of subjects given in parentheses. Sampling was done from F3-C3 leads.

(Table 5). The mentally retarded children under 18 months had definitely decreased spindle activity, and those who were 19-40 months old had increased spindle activity in comparison to normal children (Table 1). With the exception of a decrease in spindle-wave frequency, they did not show a developmental change of spindle activity.

Theoretical Considerations

Sleep spindle activity is postulated to be dependent on the intralaminar thalamic nuclei (Ralston and Ajmone-Marsan, 1956), frontal cortex (Velasco and Lindsley,

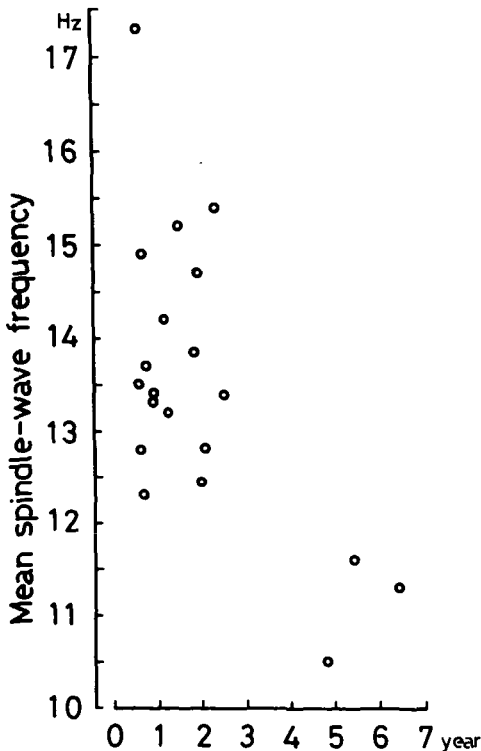


FIG. 4. Mean spindle-wave frequency as a function of age in mentally retarded children. A clear difference in mean spindle-wave frequency (Hz) can be seen when children 4-6 years of age are compared to children between birth and 2 years.

TABLE 5. Sleep spindle activity during stage 2 sleep measured from F3-C3 leads in mentally retarded children, classified into four age groups according to Tanguay et al. (1975)

Mean values	Age group (months)			
	4-7	8-18	19-40	55-68
Spindle time during stage 2 sleep				
A	0.9 (7)	2.4 (10)	0.8 (15)	3.7 (2)
B	2.2 (3)	3.0 (8)	2.0 (6)	3.7 (2)
Number of spindles/10 sec stage 2 sleep				
A	0.098 (7)	0.251 (10)	0.098 (15)	0.415 (2)
B	0.230 (3)	0.314 (8)	0.244 (6)	0.415 (2)
Spindle-burst length (sec)				
B	1.05 (3)	0.99 (8)	0.79 (6)	1.04 (2)

A, subjects with and without spindle activity; B, subjects with spindle activity. Numbers of subjects are given in parentheses.

1965), and a complex interaction of many cortical and subcortical mechanisms (Andersson et al., 1971). If it is reasonably assumed that thalamic structures mature very early (Petre-Quadens, 1972), the increase of spindles with maturation might be attributed to the development of cortical function during the first year of life (Metcalf and Jordan, 1972). Moreover, spindles in early ontogenetic stages are produced in the cortex itself and are not dependent on thalamocortical pathways (Lenard and Ohlsen, 1972). Many studies have reported absent or decreased spindle activity under various pathological conditions (Lennox and Coolidge, 1949; Jurko and Andy, 1965; Greenberg, 1966). The presence of extreme spindles and the absence of sleep spindles therefore may be attributed to a certain lesion of the structures in cerebral cortex or thalamus. It is suggested that the findings of definitely decreased or no spindle activity and disturbed development of spindles are due to these pathological changes, since it is highly probable that these lesions may be present in mentally retarded children with various etiologies.

Conclusions

In the ontogenesis of sleep spindle activity in normal children, prespindles are already seen in neonates, but these patterns disappear with increasing age. By 3 months of age, mature spindle bursts are present in the EEG during NREM sleep. The spindle activity increases and peaks between 3 and 9 months after birth. It decreases to reach minimal activity by 27 months, remains fairly constant to 54 months, then rises again to the level seen in older children. The frequency of spindles also tends to vary with age, being lower in older children.

In the development and the disorder of sleep spindle activity in mentally retarded children, those under 18 months of age have a definitely decreased level of spindle activity in comparison to normal children. In infants aged 19-40 months, spindle activity increases in comparison to normal children, who have minimal spindle activity during this period. Thus, mentally retarded children do not show

normal developmental changes in spindle activity. The frequency of spindles tends to decrease with age in such children, as in their normal peers.

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