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ORIGINAL ARTICLE

A visual motor psychological test as a predictor to treatment in nocturnal enuresis

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Background and Aims: The neurological control of bladder function and the ability to be dry at night involves not only the acquisition of normal daytime control, but also the establishment of a circadian rhythm in vasopressin release and the ability to arouse to a full bladder during sleep. We postulated that in some children there might be a delay in maturation of the normal neurological pathways involved in establishment of nocturnal continence and examined this by using a specific neuropsychological test.

Methods: Children attending an established nocturnal enuresis clinic were examined using the Rey-Osterrieth test to assess the presence or absence of boundary errors in both copy and memory reproductions. The results of the test were scored independently and blind to the response to treatment with the vasopressin analogue DDAVP.

Results: A significant association was found between boundary type errors and response to DDAVP, with non-responders making significantly more errors. No child with three or more errors responded to DDAVP. Using this test, the ability to predict response to treatment was 70%.

Conclusions: It is postulated that the Rey-Osterrieth test, through the presence or absence of boundary errors, reflects a delay in maturation and/or a disorganisation of the retinal-hypothalamic-cortical pathways in the brain. The association previously described with growth hormone neurosecretory dysfunction syndrome would be compatible with this.

The mechanisms underlying the normal postnatal development of bladder control are not fully understood. It is clear, however, that the central nervous system must play a role in converting the process from a reflex action into one that is under voluntary control. A delay in this process has been postulated as a cause of nocturnal enuresis in some children.¹

Butler and Holland have summarised factors involved in the aetiology of nocturnal enuresis into a three systems model suggesting that the treatment of nocturnal enuresis requires an understanding of these three components: a failure to produce vasopressin at night, bladder instability, and a failure to wake to a full bladder.² Each component of the three systems may be influenced by endogenous or exogenous factors. Therefore to obtain night time continence it not only requires an intact neurological pathway as for daytime continence, but the ability to develop a circadian release of vasopressin at night and to wake from sleep if urine production exceeds bladder capacity. The aetiological factors described above suggest that a disorder in the neurological pathway at any point in the visual-hypothalamic-pituitary axis and the locus coeruleus and bladder could result in enuresis.

The Rey-Osterrieth figure test (fig 1) is a neuropsychological test devised in 1941 by Andre Rey and used in children by Osterrieth in 1946. It has been widely used in the neuropsychological and clinical psychological assessment of children, and allows assessment of a variety of cognitive processes, including planning and organisational skills and problem solving strategies, as well as perceptual, motor, and memory functions. Waber and Holmes studied children's reproduction of the Rey-Osterrieth figure and determined the developmental change children make in both copying and recalling the figure.³ Andronikoff-Sanglade *et al*, using this test, noted that specific, previously unrecognised boundary type errors, were highly concordant ($p < 0.0005$) with the growth hormone neurosecretory dysfunction syndrome.⁴ These are children who have normal growth hormone response to specific stimulation tests but have low endogenous

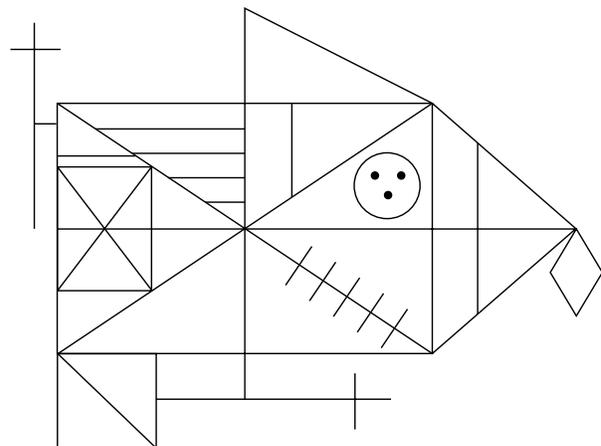


Figure 1 The Rey-Osterrieth figure.

nocturnal secretion.⁵ These boundary type errors described by Andronikoff-Sanglade *et al* are not featured as part of the normal developmental changes and were a coincidental finding when studying children with short stature. These errors were unrelated to developmental or intelligence quotient.

We postulated that some children with nocturnal enuresis might have similar findings with a neuronal developmental abnormality affecting the visual-hypothalamic-pituitary axis. The study therefore examined children with nocturnal enuresis comparing those responsive and unresponsive to treatment with the vasopressin analogue DDAVP.

METHODS

Children were recruited from an established nocturnal enuresis clinic run at Leeds General Infirmary. They were entered into the study if they fulfilled the following criteria: 7

Table 1 Description of boundary type errors in the Rey–Osterrieth figure with cut off points used in the study

Item	Item number	Description
Main rectangular structure	1	Absent (several disconnected elements scattered around)
	2	Open (one or more sides missing)
	3	Crossed by an incongruous line (discounting slight crossings at angles and junctions)
External details	4	Detached from main structure
	5	Included in main structure
Internal details	6	Entirely disconnected from adjacent elements
	7	Cross main structure boundary
	8	Placed on top of another main structural element or incongruously crossed by a line

Cut off point 1. Rey–Osterrieth figure contains one or more boundary errors in either copy or memory reproduction.

Cut off point 2. Rey–Osterrieth figure contains one or more errors in the copy reproduction only.

Cut off point 3. Rey–Osterrieth figure contains three or more boundary errors in either copy or memory reproductions.

Table 2 Details of each group

	Retrospective	Prospective	Difference
Number recruited	15	19	–
Mean age (SD)	13.3 (1.71)	9.3 (2.10)	$t=5.97$ $p<0.0001$
Male/female	12/3	14/5	Fisher exact $p=0.99$
Response to DDAVP	8	7	$\chi^2=0.38$ $p=0.54$
Number committing error (copy or memory)	8	15	Fisher exact $p=0.15$
Mean height % (SD)	57.7 (31.47)	56.6 (31.08)	$t=0.10$ $p=0.98$

Table 3 Number of children making errors

	Errors				Any
	0	1	2	3+	
Children making errors in either copy or memory reproduction					
Responds to DDAVP	8	1	6	0	7
No response to DDAVP	3	3	2	11	16
(for comparison of 0 errors with 1+ errors, Fisher exact $p=0.0301$; for comparison of 0–2 errors with 3+ errors, Fisher exact $p=0.0005$)					
Children making errors in copy reproduction only					
Responds to DDAVP	13	2	0	0	2
No response to DDAVP	5	7	4	3	14
(for comparison of 0 errors with 1+ errors, $\chi^2=9.95$, $p=0.002$)					

years or over with primary monosymptomatic nocturnal enuresis and on average greater than four wet nights per week; in fulltime education with no statement of educational need; no known neurological or urological problem; and gave informed consent. Two groups of children were entered: a retrospective group, who were already on treatment, and a prospective group, who were recruited during the study.

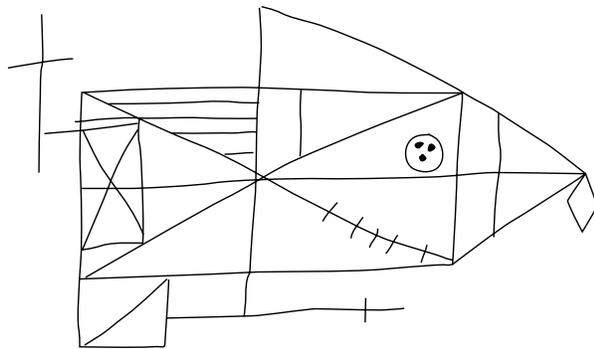
The Rey–Osterrieth figure test was administered in two parts. Firstly the child was asked to copy the figure on a blank piece of paper the same size as the model. As each section was finished, the child was handed a different coloured pencil and a note made of the colour sequence. There is no time limit for

completion. Once finished both the figure and the child's reproduction were removed from sight and approximately three minutes spent talking about unrelated issues. The child was then asked to draw the figure from memory onto a same size blank sheet of paper using a pencil with no colour change. The child is not forewarned of the task.

The figures were scored on the basis of the boundary type errors first described by Andronikoff-Sanglade and qualitative analysis of the Rey–Osterrieth figure was performed using three cut off points (table 1). One author (SB) completed the scoring after each child was allocated a random number. The author was, consequently, blind to which child was being

Table 4 Ability to predict response to treatment

	Cut off points		
	1	2	3
Sensitivity (%)	53	87	100
Specificity (%)	84	74	58
Positive predictive value (%)	73	72	65
Negative predictive value (%)	70	88	100
Likelihood ratio for positive result	3.31	3.35	2.38
Pre-test probability (%)	41	41	41
Post-test probability (%)	70	70	62

**Figure 2** Copy reproduction of the Rey-Osterrieth figure by a 12 year old boy who made no boundary type errors and responded to DDAVP.

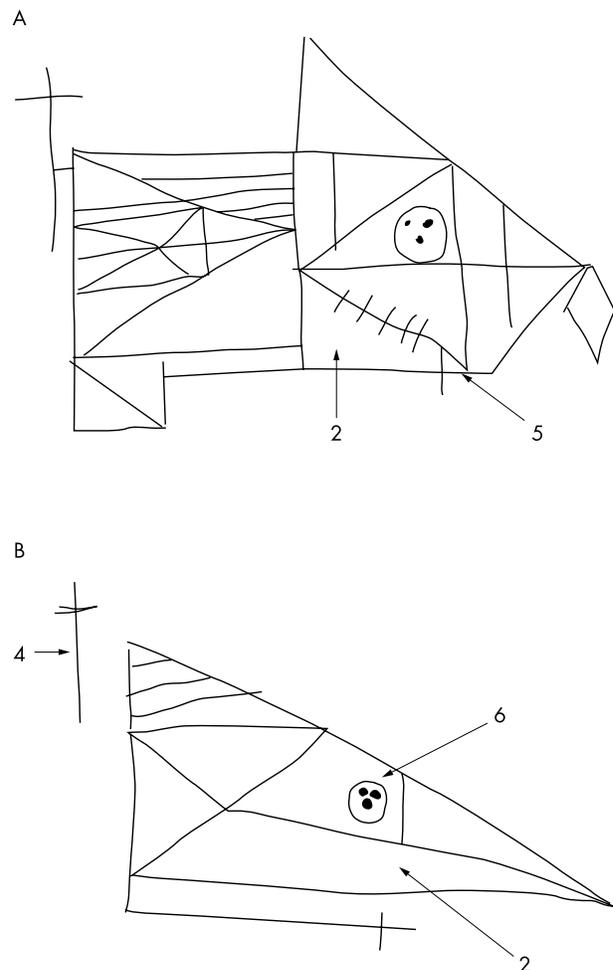
scored and did not know their response to DDAVP. Every fifth test was remarked to establish the level of intrapersonal variation in marking.

One author (PH), who was blind to the results of the psychological test, determined the child's response to treatment with DDAVP. Success was defined as more than 10 out of 14 nights on average dry, representing at least an 80% improvement in dry nights.

RESULTS

A total of 34 children were recruited to the study, 15 in the retrospective group and 19 in the prospective group. Table 2 gives details of each group. The groups differed only in terms of age, although there was no significant difference in terms of boundary type errors (Mann-Whitney test, $z = -1.21$, $p = 0.226$). The two groups were consequently combined for analysis. Although there was a significant difference between ages in the responders (12.3 years) and non-responders (10.0 years) (Mann-Whitney $z = -2.43$, $p = 0.015$), there was no significant association between age and overall number of boundary errors (Spearman $r = -0.264$, $p = 0.13$). There was no significant difference in age between those who fell above or below the three cut off points, outlined in table 1. Mean ages below and above "cut off point 1" were 11.6 and 10.8 years (Mann-Whitney $z = -0.78$, $p = 0.44$), "point 2" 11.7 and 10.3 years ($z = -1.43$, $p = 0.15$), and "point 3" 11.7 and 9.7 years ($z = -1.93$, $p = 0.054$).

A significant association was found between boundary type errors and response to DDAVP, with non-responders making significantly more errors (Mann-Whitney test, $z = -2.99$, $p = 0.003$). In both copy and memory task, 11 children (32% of 34) studied made no errors at all, four (12%) made one error, eight (24%) made two errors, and 11 (32%) made three or more errors. In copy reproduction, only 18 (53% of 34) made no error, nine (26%) made one error, four (12%) two errors, and three (9%) made three or more errors. Highly significant

**Figure 3** (A) Copy reproductions of the Rey-Osterrieth figure by a 12 year old boy who made boundary type errors and did not respond to DDAVP. (B) Memory reproduction of the Rey-Osterrieth figure with boundary type errors. The arrows indicate the type of boundary error (see table 2).

differences were found between responders and non-responders using these cut off points (table 3). No child with three or more errors responded to DDAVP. Table 4 shows the ability to predict response to treatment.

Figures 2 and 3 show the reproductions of the Rey-Osterrieth figure completed by two 12 year old boys. In fig 2 the child made no errors and responded to DDAVP. In fig 3A and B the child made errors in both the copy and memory reproductions and did not respond to DDAVP.

DISCUSSION

Andronikof-Sanglade made a chance observation during routine assessment of children with growth hormone neurosecretory dysfunction syndrome, noting specific boundary type errors on the Rey-Osterrieth test. This test is independent of development (age) or intelligence and has been validated by Andronikof-Sanglade. We postulated that this test may reflect delayed development in the neuronal pathways related to the midbrain and hypothalamic-pituitary axis, and therefore may be abnormal in children with primary enuresis. In children with nocturnal enuresis we showed that those children unresponsive to DDAVP had a highly significant increase in boundary type errors, independent of growth.

Jarvelin has reported that children with poor linear growth were more likely to have nocturnal enuresis. Devitt *et al*, using a generalised linear model analysis, showed that the shorter

the child the less likely they were to respond to DDAVP.^{6,7} Stimulation of growth and the development of nocturnal continence both depend on the night time release of growth hormone and vasopressin respectively. The establishment of these circadian rhythms depends on the maturation of neurological pathways, including the retinohypothalamic projection direct to the suprachiasmatic nucleus, the body's internal clock. The hypothalamus acts as the principal control on the production of both growth hormone via the anterior pituitary, and vasopressin via the posterior pituitary. Vasopressin is synthesised in the suprachiasmatic nucleus and is transferred, attached to its carrier protein neurophysin, down the magnocellular neurones to be stored in vesicles within the posterior pituitary. At term only about 13% of the adult number of neurones are present; this number increases rapidly over the first few months after birth and coincides with the establishment of overt diurnal rhythms.⁸ Jarvelin and Devitt *et al* have also shown an association between nocturnal enuresis and low birth weight, again suggesting the possibility of maturational delay.

Andronikoff-Sanglade postulated that these specific errors were identifying a corticohypothalamic disturbance that resulted in poor growth hormone production at night. Height was therefore included as a confounding variable to ensure that this study was not simply including children with this syndrome. The fact that no such association was found suggests that this was not the case. Interestingly, in this study the presence of boundary type errors was much more sensitive to the child's current ability to respond, rather than their ability in the past, suggesting an ability of the system to mature with time. Linking this study to that of Andronikoff-Sanglade suggests a maturational delay in the retinal-hypothalamic pituitary axis that can potentially be detected using the Rey-Osterrieth test. We postulate that pre- and postnatal factors at a crucial period of neuronal development affect the maturation of neurones in the midbrain and hypothalamus, manifesting as a delay in growth and attainment of nocturnal

continence. An understanding of the factors, whether environmental or genetic, which contribute to this may result in a better understanding of the management of nocturnal enuresis. If these studies are replicated, they are potentially important in defining a treatment programme for the older child with enuresis, although the results should be viewed in context of an increasing understanding of the pathophysiology of nocturnal enuresis.

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