### La sindrome di Angelman: il problema delle crisi

- Crisi o non crisi? Questo è il problema....
- Pedagogia dell'anamnesi: ovvero come raccontare una crisi al medico, sperando che non vada fuori strada...
- L'inizio della terapia AE: necessità ed abusi (ovvero, la punta-onda fa sempre male?)
- La scelta del farmaco "giusto": le scienze di base ci aiutano veramente in questo?

### Definizioni

- Crisi epilettica: manifestazione clinica di una scarica neuronale persincrona, di durata variabile, autolimitantesi, che interessa in modo prevalente la corteccia cerebrale
- presentazione, caratterizzata dalla ripetizione di crisi epilettiche non sintomatiche di una lesione acuta del sistema nervoso Epilessia: sindrome clinica, eterogenea per eziologia e
- un evidente evento patologico immediatamente precedente, Crisi sintomatica acuta: crisi epilettica conseguente ad cerebrale o sistemico; può costituire un evento isolato
- Crisi sintomatica remota: crisi epilettica conseguente ad una pregressa lesione cerebrale
- si manifesta come crisi prolungata o crisi seriate senza ricupero Stato di male epilettico: attività epilettica persistente che tra l'una e l'altra



## **Crisi autolimitanti**

- generalizzate
- focali

- stato epilettico generalizzato
- stato epilettico focale





## Crisi autolimitanti

- generalizzate
- focali

- stato epilettico generalizzato
- stato epilettico focale

- tonico-cloniche
- cloniche
- assenze tipiche
- assenze atipiche
- assenze miocloniche
- toniche
- spasmi
- miocloniche
- mioclonie palpebrali
- mioclonico-atoniche
- mioclono negativo
- atoniche



## Crisi autolimitanti

- generalizzate
- focali

- stato epilettico generalizzato
- stato epilettico focale

- sensoriali -
- motorie
- gelastiche
- emicloniche
- secondariamente generalizzate
- con sintomi sensoriali elementari (es. occipitali)
- con sintomi sensoriali
   esperienziali (es. temporoparieto-occipitali)



## Crisi autolimitanti

- generalizzate
- focali

- stato epilettico generalizzato
- stato epilettico focale

- sensoriali
- motorie -
- gelastiche
- emicloniche
- secondariamente generalizzate
- · cloniche elementari
- toniche asimmetriche
- con automatismi tipici (lobo temporale)
- con automatismi ipercinetici
  - mioclono negativo focale motorie inibitorie



## Crisi autolimitanti

- generalizzate
- focali

## Crisi continue

- stato epilettico generalizzato
- stato epilettico focale

- tonico-clonico

- clonico

- di assenza

- tonico

- mioclonico



## Crisi autolimitanti

- generalizzate
- focali

- stato epilettico generalizzato
- stato epilettico focale

- epilessia parziale continua di Kojevnikov
- · aura continua
- stato epilettico limbico (stato psicomotorio)
- stato emiconvulsivo con emiparesi



### Mioclono corticale

Mioclono non corticale

### Myoclonus in Angelman syndrome: is it always of cortical origin?

Maurizio Elia, Raffaele Ferri, Maria Bottitta, Paolo Bosco, Sebastiano A. Musumeci

(presented at the 1st World Conference of the International Angelman Syndrome Organization, Tampere Finland, July 4-8, 2000)

Fifteen subjects with AS (7 males, age range 4 - 26 years, mean age 11.64 years, DS 6.61 years) were included in this study

Back averaging of EEG interictal activity related to EMG potentials was performed in all cases; in 11 subjects median nerve somatosensory evoked potentials (SEPs) were recorded and the eventual presence of C-reflex assessed Only in two subjects, both of them with deletion of the region 15q11-13, a negative cortical wave 60 to 75 milliseconds before the myoclonic jerk was found. No 'giant' SEPs or C-reflex were found

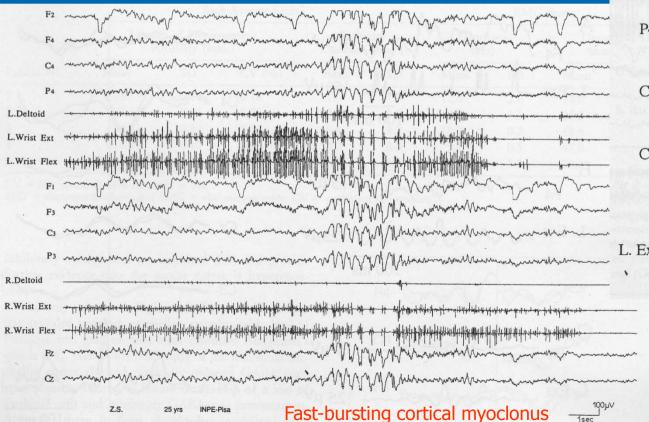
Our findings allow us to exclude the presence of a cortical reflex myoclonus in AS

### Cortical Myoclonus in Angelman Syndrome

Renzo Guerrini, MD,\* Timothy M. De Lorey, PhD,† Paolo Bonanni, MD,\* Anne Moncla, MD,‡ Charlotte Dravet, MD,§ Georges Suisse, MD,<sup>1</sup> Marie Odile Livet, MD,§ Michelle Bureau, MD,§ Perrine Malzac, PhD,‡ Pierre Genton, MD,§ Pierre Thomas, MD,<sup>1</sup> Ferdinando Sartucci, MD,<sup>1</sup> Paolo Simi, PhD,<sup>‡</sup> and José M. Serratosa, MD†

Angelman syndrome (AS) results from lack of genetic contribution from maternal chromosome 15q11–13. This region encompasses three GABA<sub>A</sub> receptor subunit genes ( $\beta$ 3,  $\alpha$ 5, and  $\gamma$ 3). The characteristic phenotype of AS is severe mental retardation, ataxic gait, tremulousness, and jerky movements. We studied the movement disorder in 11 AS patients, aged 3 to 28 years. Two patients had paternal uniparental disomy for chromosome 15, 8 had a >3 Mb deletion, and 1 had a microdeletion involving loci D15S10, D15S113, and GABRB3. All patients exhibited quasicontinuous rhythmic myoclonus mainly involving hands and face, accompanied by rhythmic 5- to 10-Hz electroencephalographic (EEG) activity. Electromyographic bursts lasted 35  $\pm$  13 msec and had a frequency of 11  $\pm$  2.4 Hz. Burst-locked EEG averaging in 5 patients, generated a premyoclonus transient preceding the burst by 19  $\pm$  5 msec. A cortical spread pattern of myoclonic cortical activity was observed. Seven patients also demonstrated myoclonic seizures. No giant somatosensory evoked potentials or C-reflex were observed. The silent period following motor evoked potentials was shortened by 70%, indicating motor cortex hyperexcitability. Treatment with piracetam in 5 patients significantly improved myoclonus. We conclude that spontaneous, rhythmic, fast-bursting cortical myoclonus is a prominent feature of AS.

Guerrini R, De Lorey TM, Bonanni P, Moncla A, Dravet C, Suisse G, Livet MO, Bureau M, Malzac P,
Genton P, Thomas P, Sartucci F, Simi P, Sertatosa JM. Cortical myoclonus
in Angelman syndrome. Ann Neurol 1996;40:39–48



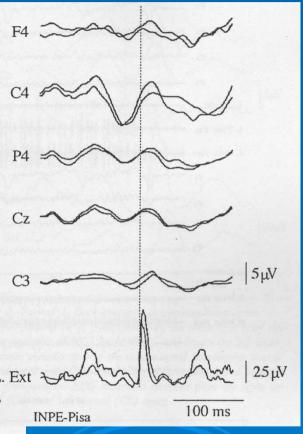
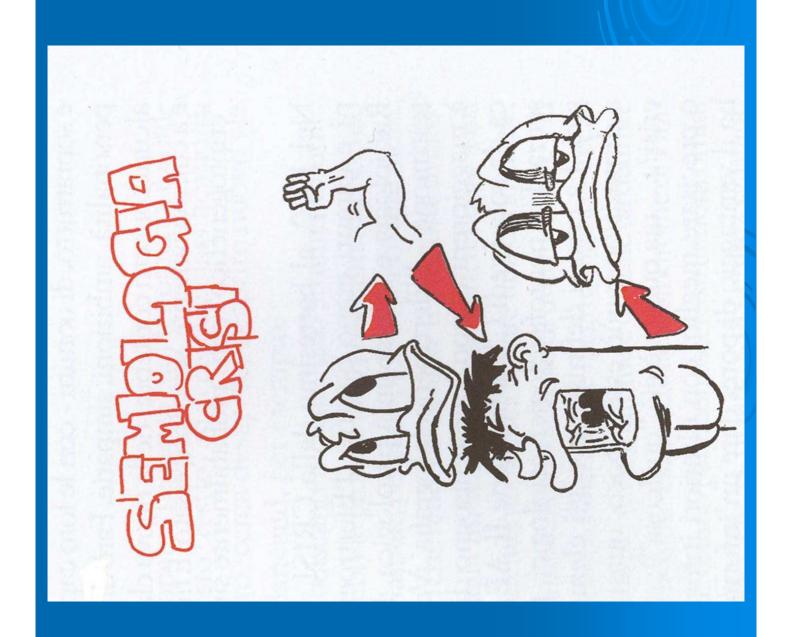


Table 1 Comparison between AS patients aged less than 15 (group A) and age-matched normal controls (group C)	oup A) and age-matched nor	mal controls (group C)		
	Group C (%)	Group A (%)	Chi-square	P <
Radition machines				
1. Sleep less than 8 h	9.63	70.27	117.68	0.00001
2. Latency to sleep > 30 min	19.9	32.43	30.04	0.00001
3. Reluctant to go to bed	29.68	59.46	13.41	0.003
4. Bedtime variations	38.63	48.65	11.1	NS
<ol><li>Difficulty getting to sleep at night</li></ol>	8.96	56.76	78.98	0.00001
6. Anxiety/fear when falling asleep	8.17	43.24	46.52	0.00001
7. Drink stimulant beverages in the evening	27.32	27.03	0.02	SN
8. Need for light or TV in the bedroom	27.21	32.43	0.26	SN
9. Need for a transitional object	18.25	48.65	19.05	0.00001
<ol> <li>Fluids or drugs to facilitate sleep</li> </ol>	29.0	32.43	172.46	0.00001
Sleep-wake transition disorders				
11. Hypnic jerks	5.04	59.46	149.35	0.00001
<ol> <li>Rhythmic movements while falling asleep</li> </ol>	2.69	27.03	53.04	0.00001
13. Falling askep sweating	10.30	13.51	0.12	SN
Sleep quality				
14. Poor sleep quality	13.89	70.27	79.38	0.00001
Night awakenings				
<ol><li>More than two awakenings per night</li></ol>	6.83	62.16	125.73	0.00001
<ol><li>Waking up screaming in the night</li></ol>	5.49	18.92	9.08	0.003
<ol><li>Waking up to drink or eat in the night</li></ol>	13.55	24.32	2.59	SN
<ol><li>Getting up to use to the bathroom</li></ol>	10.64	2.70	1.64	SN
<ol> <li>Difficulty to fall asleep after awakenings</li> </ol>	4.82	56.76	141.58	0.00001
20 Nocturnal hyperkinesias	29 00	15 19	23.12	0 000001
21. Unusual movements during sleep	5.94	48.65	85.96	0.00001
22. Pains of unknown origin during sleep	0.56	×c	35 X	100000
23 Convalsions during sleen	290	5.41	4.61	0.035
Sleen breathing problems		•		*****
24. See breathing difficulties	6.83	18.92	5.98	0.015
25 Shen spines	101	2.20	0.03	SN
26 Snoring	14.67	32.43	7.30	0000
Parasonnias				
27. Night sweating	15.90	18.92	0.07	NS
28. Sleepwalking	3.14	5.41	0.08	SN
29. Sleep talking	14.45	2.70	3.16	SN
30. Bed-wetting	2.35	35.14	99.30	0.00001
31. Bruxism	7.39	21.62	7.98	0.005
32. Skep terrors	1.34	5.41	1.69	SN
33. Nightmares	10.64	0.00	3.30	SN
Morning symptoms				
34. Difficulty in waking up in the morning	35.95	35.14	0.01	SN
35. Variation of waking time	25.87	37.84	2.04	SN
36. Skep paralysis	4.14	13.51	5.22	0.025
Daytime sleepiness				
37. Daytime sonnolence	4.48	24.32	24.20	0.00001
38. Falling askep at school	0.34	8.11	22.45	0.00001
39. Skep attacks	1.40	2.70	0.01	NS

Redultione probletome 1         20.27         50.00         0.57         NS           1. Lakeep to solate 3         2.4.4         5.0.0         0.02         NS           4. Redusemat to go to bead with a solate 3 - 50 min to step 3 - 50 min to st		Group A (%)	Group B (%)	Chi-square	P <
8 by 10 color of the color of t					
by 8 h h h h h h h h h h h h h h h h h h	Bedtime problems				
sape > 30 min         32.43         25.00         0.02           sp to bed         sp to bed         32.44         5.00         0.02           sp to bed         sp to bed         48.65         25.00         0.06           sing to sheep at night         48.67         33.33         0.06           sing to sheep at night         48.63         3.03         3.43           at beverages in the evening         27.03         3.03         3.45           at the bedroom         32.43         3.33         3.06           age to facilitate sleep         32.43         3.00         0.06           as to be facilitate sleep         27.03         25.00         0.06           section disorder         3.44         5.00         0.06           section disorder         3.43         0.06         0.06           section disorder         3.44         3.00         0.06           section disorder         3.24         3.20         0.06           section disorder         3.24         3.24         3.33         4.62           section disorder         3.24         3.25         0.00         0.00           section disorder         3.24         3.25         0.00         0.00 <td>1. Skep less than 8 h</td> <td>70.27</td> <td>90.00</td> <td>0.87</td> <td>NS</td>	1. Skep less than 8 h	70.27	90.00	0.87	NS
special bodies         \$9.46         \$0.00         0.06           stricts         48.65         55.00         0.06           stricts         48.65         58.33         0.05           when flight askep         27.03         0.00         0.06           was analyzed in the bedroom         32.43         33.33         0.57           nentioned beject         48.65         8.33         0.07           station disorders         32.43         30.00         0.00           station disorders         59.46         25.00         0.00           station disorders         59.46         25.00         0.00           station disorders         59.46         25.00         0.00           station disorders         27.03         25.00         0.00           ps swearing         6.216         25.00         0.00           ps swearing         6.216         33.33         0.00           ps swearing         13.51         16.67         0.02           ps swearing         13.51         43.25         0.00           ps swearing         14.67         0.00         0.00           ps swearing         14.67         0.00         0.00           ps	2. Latency to sleep > 30 min	32.43	25.00	0.02	NS
Section   Sect	3. Reluctant to go to bed	59.46	50.00	90.0	NS
sing of the percenting a deep at night a deep a deep at night a deep at night a deep a deep at night a deep a d	4. Bedtime variations	48.65	25.00	1.22	NS
weben fulling aslesp         43.34         8.33         3.45           weben fulling aslesp         27.03         8.33         3.45           austional object         32.43         33.33         3.45           sational collection         32.43         33.33         3.45           sation alternal esep         32.43         3.00         0.09           sation alternal esep         27.03         25.00         0.06           sation alternal esep         27.03         25.00         0.06           ps swearing         27.03         25.00         0.06           ps wearing         27.23         66.67         0.04           ps wearing         27.23         66.67         0.04           ps wearing         27.23         66.67         0.00           ps wearing         27.23         25.00         0.00           ps we awakenings per night         27.25         25.00         0.00           ps wearing         27.25         25.00         0.00           ps wearing         27.25         25.00         0.00           ps wearing with the night         27.25         25.00         0.00           ps wearing almost states         27.43         27.00         0	<ol><li>Difficulty getting to sleep at night</li></ol>	56.76	58.33	90.0	NS
and the evening of the bedroom         27.93         0.00         2.58           and belochman size along askep         32.43         33.33         0.57           askion allowide rs         32.43         33.33         0.67           ask of all interesting askep         27.03         25.00         0.09           overneants while falling askep         27.03         25.00         0.06           a swearing         13.51         16.67         0.03           a swearing as in the night         62.16         38.33         0.01           a creaming in the night         27.0         8.33         0.01           a creaming in the night         27.0         8.33         0.00           a creaming in the night         27.0         8.33         0.01           a creaming in the night         27.0         8.33         0.00           fall salesp after awakenings         56.76         41.67         0.00           fall salesp after awakenings         56.76         41.67         0.00           fall salesp after awakenings         67.5         75.00         0.00           fall salesp after awakenings         67.5         75.00         0.00           fall salesp after awakenings         67.5         75.00	6. Anxiety/fear when falling asleep	43.24	99.33	3.45	0.1 > P > 0.05
tor TV in the bedroom 32,43 33,33 0,57 minimitional object 48,65 8,33 0,00 0,00 on object 68,65 0,00 0,00 0,00 on object 68,65 0,00 0,00 0,00 on object 68,65 0,00 0,00 0,00 0,00 0,00 0,00 0,00 0	7. Drink stimulant beverages in the evening	27.03	0.00	2.58	NS
respect object         48.65         8.33         4.62           stood floratest eleep         32.43         50.00         0.09           stood floratest eleep         32.43         50.00         0.09           stood floratest eleep         27.33         25.00         0.00           ps swearing         70.27         66.67         0.02           ps wearing and ps registr         62.16         38.33         0.00           to use to the batheroon         27.0         8.33         0.00           por string sleep         66.67         0.00         0.00           por tink or sat in the night         18.22         25.00         0.00           to use to the batheroon         2.70         8.33         0.00           o use to the batheroon         2.70         8.33         0.00           one of the batheroon         2.70         8.33         0.00           near to the batheroon         2.70         8.33         0.00           o use to the batheroon         0.07         1.12         0.00           o use to the batheroon         0.07         1.27         0.00           o use to the batheroon         0.07         1.27         0.00           parking sleep <t< td=""><td>8 Need for light or TV in the bedroom</td><td>32.43</td><td>33 33</td><td>0.57</td><td>SN</td></t<>	8 Need for light or TV in the bedroom	32.43	33 33	0.57	SN
and the contents while falling asleep 27.03 50.00 0.09  anality 27.03 25.00 0.06  p sweating lefuling asleep 27.03 25.00 0.00  anality 70.27 66.67 0.00  anality 70.27 66.67 0.00  anality 70.27 66.67 0.00  anality 70.27 66.67 0.00  anality 70.29 38.33 0.00  and the night 24.32 0.00 0.00  and the cereaning in the night 24.32 0.00  and the cereaning in the night 34.00  and the cereaning in the norming 24.40  and the cereaning in the norming 35.44 0.00  and the cereaning	9. Need for a transitional object	48.65	8.33	4.62	SN
section disorders         59.46         25.00         3.04           sexue acting         70.27         66.67         0.04           ps weakings per might         62.16         38.33         0.01           op awakenings per might         62.16         38.33         0.01           op awakenings per might         62.16         38.33         0.01           op awakenings per might         62.16         38.33         0.01           op acting or cat in the night         24.32         25.00         0.00           o tast or the bathroom         2.70         48.53         0.00           o tast or the bathroom         2.70         48.53         0.00           o tast or the bathroom         2.70         48.67         0.00           predictions after awakenings         56.76         41.67         0.00           predictions after awakenings         48.65         25.00         0.00           problems         48.65         25.00         0.00           g         2.70         16.67         0.00           g         2.70         16.67         0.00           g         2.70         0.00         0.36           g         2.70         0.00         0.36 </td <td>10. Fluids or drugs to facilitate sleep</td> <td>32.43</td> <td>20.00</td> <td>000</td> <td>SN</td>	10. Fluids or drugs to facilitate sleep	32.43	20.00	000	SN
s yeads         25.00         3.04           overnents while falling seleep         27.03         25.00         0.06           ps sweating         70.27         66.67         0.02           gs sweating in the night         18.92         25.00         0.01           exeraming in the night         18.92         25.00         0.01           exeraming in the night         18.92         0.00         2.14           exeraming in the night         27.0         8.33         0.01           fall select and wakenings         56.76         41.67         0.03           fall select partitions are selected as wakenings         67.57         75.00         0.02           fall select partitions are selected as wakenings         67.57         75.00         0.02           fall select partitions are selected as wakenings         66.7         5.00         0.02           fall select partitions are selected as a se	Sleep-wake transition disorders		A Control of	Za.a.	
overnents while falling salesp 27.03 25.00 0.06 anality 13.51 16.67 0.04 anality 2.03 13.51 16.67 0.04 0.04 anality 2.03 13.51 16.67 0.04 0.00 0.00 0.00 0.00 0.00 0.00 0.0	11 Hunnic leafes	50.46	35.00	3.04	0.1 > P > 0.05
anality to the beachers of the control of the contr	12. Rhythmic movements while falling scleen	27.03	25.00	900	NS
radiity  vo awakenings per night  versaming in the night  tereaming in the night  tereaming in the night  2432  25.00  b drink or eat in the night  2432  25.00  cereaming in the night  2432  25.00  2.14  4.167  4.167  2.14  4.167  4.167  4.167  4.167  4.161  4.	13 Falling schon experting	13.51	16.67	0.04	SN
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or awakenings per night         62.16         58.33         0.01           cereaming in the night         18.92         25.00         0.00           be dried or earl in the night         2.432         0.00         2.14           fall asleep after awakenings         56.76         41.67         0.33           nexit during sleep         67.57         75.00         0.02           speckinesias         67.57         75.00         0.02           speckinesias         67.57         5.00         1.22           speckinesias         66.7         5.00         0.02           speckinesias         67.7         5.00         0.02           speckinesias         67.7         5.00         0.02           speckinesias         67.7         5.00         0.02           during skep         66.7         5.41         4.61           problems         18.92         1.67         0.06           g         2.70         0.00         0.35           g         2.70         0.00         0.35           g         2.70         0.00         0.31           g         2.14         41.67         0.00           g         2.16         8.	Nicht ausdening	15.01	00:07	0.02	CVI
reconnenting in the might  2432  25.00  o use to the bathroom  270  41.67  61.33  fall asleep after awakenings  for its sleep	regard are accounted as 15 Move than two sureleminos nor night	9109	48 33	100	SN
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Marketing barmoon   2.70   0.33     All asleep after awakenings   56.76   41.67   0.33     All asleep after awakenings   56.76   41.67   0.00     Aperkinesias   67.57   75.00   0.00     Aperkinesias   67.57   75.00   0.00     Aperkinesias   67.57   75.00   0.00     Aduring sleep   48.65   25.00   0.23     Aduring sleep   67.57   27.00   0.00     Aduring sleep   67.57   27.00   0.00     Aduring sleep   67.57   0.00     Aduring sleep   67.57   0.00   0.35     Aduring sleep   67.57   0.00   0.36     Aduring sleep   67.57   0.00   0.36     Aduring sleep   67.57   0.00   0.36     Aduring sleep   67.57   0.00     Aduring sl	17. Waking up to drillik or ear in the ingin	24.72	0.00	2 00 0	SN
range during along and awatenings         50.70         41.67         0.53           speckinesis as during along vennents during sleep         48.65         25.00         0.02           owner unique along along during sleep         48.65         25.00         1.22           owner unique along along during sleep         0.67         5.41         4.61           problems         18.92         16.67         0.06           ing difficulties         18.92         0.00         0.57           ing difficulties         18.92         0.00         0.36           g         5.41         16.67         0.40           g         5.41         8.33         0.11           g         5.41         8.33         0.01           masking time         35.14         41.67         0.00           wasking time         37.84         25.00         0.00           exs         9 at school         0.00         0.00           p at school         27.0         0.00         0.3	to recentling up to use to the nationality	07.7	6.53	0.00	SN
regently attempt steep 67.57 75.00 0.02 comments during sleep 48.65 25.00 1.22 comments during sleep 6.67 5.41 4.61 comments during sleep 0.67 5.41 4.61 comments during sleep 0.67 5.41 4.61 comments difficulties 18.92 16.67 1.12 comments comments 18.92 0.00 1.33 comments 18.92 0.00 0.36 comments 5.41 16.67 0.40 0.36 comments 5.41 16.67 0.00 0.36 comments 5.41 8.33 0.36 comments 5.41 8.33 0.36 comments 5.41 41.67 0.00 comments 5.41 41.67 0.00 comments 5.42 comments 5.43 0.00 comments	19. Difficulty to fall asleep after awakenings	20.70	41.0/	0.33	SS
operations         of 3.7         7.5.00         0.02.           venents during sleep         48.65         25.00         1.22           venents during sleep         667         5.41         4.61           problems         18.92         16.67         0.06           problems         18.92         16.67         0.06           ing difficulties         18.92         16.67         0.05           ing difficulties         18.92         0.00         0.57           ing         18.92         0.00         0.57           ing         18.92         0.00         0.57           ing         5.41         16.67         0.40           g         5.41         16.67         0.40           g         5.70         0.00         0.35           g         5.41         8.33         0.11           max         41.67         0.00           wasking une         37.84         25.00         0.00           ess         13.51         8.33         0.00           ess         18.33         0.34           p at school         2.70         0.00         0.36           g         4.1.67         0.00 <td>20 Months movements annug steep</td> <td>63.63</td> <td>50</td> <td>000</td> <td>NIG</td>	20 Months movements annug steep	63.63	50	000	NIG
vennents during sleep         48.65         25.00         1.22           new reign during sleep         1601         5.41         4.61           reducing sleep         1892         1667         0.06           ing difficulties         1892         1667         0.06           ing difficulties         1892         1667         0.06           ing         2.70         0.00         0.57           ing         2.41         1667         0.40           g         5.41         1667         0.40           g         5.41         50.00         0.33           s         5.41         8.33         0.11           waxing up in the morning         35.14         50.00         0.33           waxing time         37.84         25.00         0.21           sis         13.51         8.33         0.00           exp         9 at school         9.34           s         10.00         0.36           one         1.667         0.02           one         0.00         0.34           one         0.00         0.36           one         0.36         0.36           one         0.00 <td>20. Noctumal hyperkinesias</td> <td>1510</td> <td>75.00</td> <td>0.02</td> <td>SN</td>	20. Noctumal hyperkinesias	1510	75.00	0.02	SN
during skep         067         5.41         4.61           problems         1892         16.67         0.06           ing difficulties         1892         16.67         0.06           ing         1892         0.00         0.57           ing         1892         0.00         0.57           ing         1892         0.00         0.35           g         5.41         16.67         0.40           g         2.70         0.00         0.36           g         2.70         0.00         0.35           s         35.14         50.00         0.35           waxing up in the morning         35.14         8.33         0.11           waxing time         37.84         25.00         0.21           s is         13.51         8.33         0.00           a stabool         24.15         0.00         0.34           p at school         8.11         8.33         0.34           s         0.00         0.36           o         0.00         0.36	21. Unusual movements during sleep	48.65	25.00	1.22	NS
ing difficulties  1892 1667 270 1667 270 1667 1.12 32.43 1892 1667 1.12 1.12 32.43 1892 0.00 0.57 1.13 8 8 8 8 8 8 8 8 8 8 8 8 8 8 8 8 8 8 8	23. Convalsions during sleep	290	5.41	4.61	0.035
ing difficulties 1892 16.67 0.06  270 16.67 1.12  32.43 50.00 0.57  ing Edifficulties 1892 0.00 0.57  g 5.41 16.67 0.40  g 5.41 50.00 0.33  straight in the morning 35.14 8.33 0.11  waking time 37.84 25.00 0.21  sis extra 13.51 8.33 0.00  extra p at school 8.11 8.33 0.36  s s s chool 8.11 8.33 0.34  s s s chool 8.11 8.33 0.34  s s s chool 8.11 8.33 0.34  s s s chool 8.31 8.33 0.35  s s chool 8.31 8.33 0.36	Sleen breathing problems				and the second
ring 18.92 16.67 1.12 2.70 18.92 0.00 0.57 1.12 2.43 50.00 0.57 1.12 2.44 50.00 0.36 0.36 0.36 0.36 0.36 0.36 0.36	24 Shen bresthing difficulties	18 92	19 91	90 0	SN
ng 18.92 0.00 0.57 (1.33) g 5.41 16.67 0.40 (1.33) g 5.41 16.67 0.40 (1.33) g 5.41 16.67 0.40 (1.33) g 5.41 8.33 0.36 (1.33) over statementing 35.14 8.33 0.00 (1.33) sis 13.51 8.33 0.00 (1.35) another e 24.32 16.67 0.00 (1.35) s at school 8.11 8.33 0.34 (1.67) s at school 8.11 8.33 0.34	25 Chem annea	270	16.67	1.13	SN
18.92     0.00     1.33       5.41     16.67     0.40       2.70     0.00     0.36       35.14     50.00     0.35       21.62     8.33     0.36       5.41     8.33     0.11       0.00     0.00     0.00       king time     37.84     25.00     0.21       slence     24.32     16.67     0.02       stepool     8.11     8.33     0.34       t school     2.70     0.00     0.36	26. Snoring	32.43	20.00	0.57	SN
18.92     0.00     1.33       5.41     16.67     0.40       2.70     0.00     0.36       35.14     \$0.00     0.33       21.62     8.33     0.36       5.41     8.33     0.11       0.00     0.00     0.01       king time     37.84     25.00     0.21       slence     24.32     16.67     0.02       strood     8.33     0.34       t school     2.70     0.00     0.36	Parassenias				
5.41     16.67     0.40       2.70     0.00     0.36       35.14     50.00     0.36       21.62     8.33     0.36       5.41     8.33     0.11       bring up in the morning     35.14     41.67     0.00       bring time     37.84     25.00     0.21       13.51     8.33     0.00       a school     8.11     8.33     0.34       270     0.00     0.36	27. Night sweating	18.92	0.00	1.33	SN
2.70 0.00 0.36 35.14 50.00 0.36 35.14 50.00 0.36 21.62 8.33 0.36 5.41 8.33 0.11 0.00 0.00 saking up in the morning 35.14 41.67 0.00 sis solutions 37.84 25.00 0.21 sis notence 24.32 16.67 0.02 at school 2.70 0.00 0.36	28. Sleenwallting	5.41	16.67	0.40	SN
35.14 50.00 0.33 21.62 8.33 0.36 5.41 8.33 0.11 0.00 0.00 waking up in the morning 35.14 41.67 0.00 waking time 37.84 25.00 0.21 sis nolence 24.32 16.67 0.02 as school 8.11 8.33 0.34 2.70 0.00 0.36	29. Sleep talking	2.70	0.00	0.36	NS
21.62 8.33 0.36  5.41 8.33 0.36  9.00 0.00  waking up in the morning 35.14 41.67 0.00  waking time 37.84 25.00 0.21  is 13.51 8.33 0.00  an oleance 24.32 16.67 0.02  at school 2.70 0.00 0.36	30. Bed-wetting	35.14	20 00	0.33	SN
Nating up in the morning 35.14 41.67 0.00 waking time 33.84 25.00 0.21 37.84 25.00 0.21 37.84 25.00 0.21 an oleance 24.32 16.67 0.02 art school 2.70 0.00 0.00 0.36	31. Bruxism	21.62	8.33	0.36	NS
ma waking up in the morning 35.14 41.67 0.00 waking time 33.14 25.00 0.21 3.51  8.33 0.00 3.51  9.51  13.51 8.33 0.30	32. Sleen terrors	541		0.11	SN
35.14 41.67 0.00 37.84 25.00 0.21 13.51 8.33 0.00 24.32 16.67 0.02 8.11 8.33 0.34 2.70 0.00 0.36	33. Nightmares	000	0.00		1
35.14 41.67 0.00 37.84 25.00 0.21 13.51 8.33 0.00 24.32 16.67 0.02 8.11 8.33 0.34 2.70 0.00 0.36	Morning symptoms				
37.84     25.00     0.21       13.51     8.33     0.00       24.32     16.67     0.02       8.11     8.33     0.34       2.70     0.00     0.36	34. Difficulty in waking up in the morning	35.14	41.67	0.00	NS
13.51 8.33 0.00 24.32 16.67 0.02 8.11 8.33 0.34 2.70 0.00 0.36	35. Variation of waking time	37.84	25.00	0.21	NS
2432 16.67 0.02 8.11 8.33 0.34 2.70 0.00 0.36	36. Sleep paralysis	13.51	8.33	0.00	NS
2432 16.67 0.02 8.11 8.33 0.34 2.70 0.00 0.36	Daytime sleepiness				
8.11 8.33 0.34 2.70 0.00 0.36	37. Daytime sonnolence	24.32	16.67	0.02	SN
2.70 0.00 0.36	38. Falling askep at school	8.11	8.33	0.34	NS
	39. Skep attacks	2.70	0.00	0.36	NS

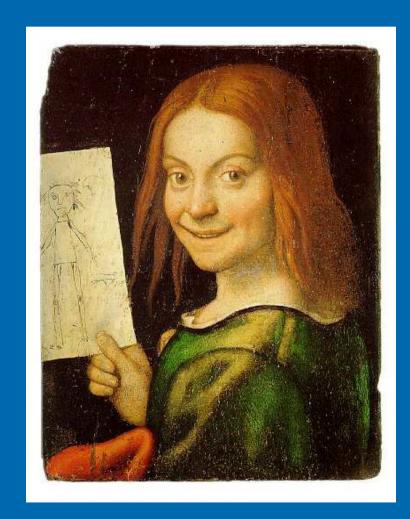


Develop. Med. Child Neurol. 1965, 7, 681-688

'Puppet' Children
A Report on Three Cases

Harry Angelman

"Very frequently fits resembling a hypsarrhythmic state and a profound degree of mental retardation"



### Seizures

- > 31/34 subjects (91.2%) with seizures
- > 2 of the patients without seizures had a mutation in UBE3A, 1 had UPD
- age at onset of seizures ranged from 1 month to 5 years (mean 1.92, SD 1.33)
- > 17/31 subjects (54.83%) were seizure-free at the last visit; 2 of them took no AEDs at that time; recent data were not available for 1 subject (#21)
- > age at the last seizure ranged from 1 to 28 years (mean 10.47, SD 7.99)
- decreasing the dosage of AEDs in 2 patients led to recurrence of seizures (#1, #26)

### **Epilepsy in patients with 15q11-13 deletion**

	Matsumoto et al., 1992	Sugimoto et al., 1992	Viani et al, 1995	Guerrini et al., 1996	Rubin et al., 1997	Laan et al., 1997	Minassian et al., 1998	Our series
No. of cases/M	8/3	3/2	18/13	9/3	3/3	36/20	9/4	20/12
Epilepsy	8/8	3/3	15/18 (83.3%)	9/9	3/3	30/36 (83.3%)	9/9	20/20
Typical EEG	8/8	3/3	18/18	9/9	3/3	30/36 (83.3%)	9/9	20/20
Age (last follow-up)	4-26 yrs (15.63 ±6.63)	1-6 yrs (3.33 ±2.52)	1-28 yrs (7.97 ± 7.00)	3-28 yrs (18.44 ±8.07)	1-3 yrs (2.39 ±0.72)	1yr 6 mos-39 yrs (11)	2-41 yrs (17.11± 15.03)	2-32 yrs (16.36 ± 8.58)
Age at seiz. onset	3 mos-3 yrs (1.32 ±0.9)	1 yr 2 mos-1 yr 7 mos	9 mos-4 yrs 10 mos	4 mos-5 yrs (1.42 ±1.59)	1 -2 yrs (1.72 ±0.24)	1 mo-5 yrs (2)	6 mos-2 yrs (0.93 ± 0.62)	1 mo-5 yrs (1.46 ±1.21)
Myocloni c status	4/8 (50%)	1/3 (33%)	13/15 (86.7%)	4/9 (44.4%)	1/3 (33.3%)	5/30 (16.7%)	1/9 (11.1%)	9/20 (45%)
Seizure- free (last visit)	7/8 (87.5%)	?	?	?	?	5/13 (38.5%)	0/9	11/19 (57.9%)

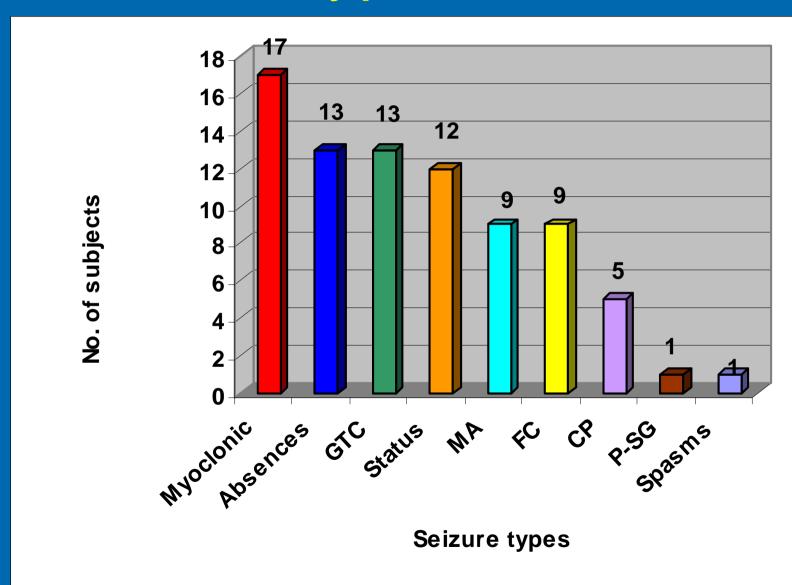
### **Epilepsy in patients with UPD**

	Guerrini et al., 1996	Minassian et al., 1998	Our series
No. of cases/M	2/2	4/4	4/2
Epilepsy	1/2 (50%)	2/4 (50%)	3/4 (75%)
Typical EEG	2/2	3/4 (75%)	4/4
Age (last follow- up)	7-15 yrs	7-15 yrs (11.25 ± 4.34)	3-15 (11.06 ± 5.48)
Age at seizure onset	4 yrs	?	2-5 yrs (3.33 ± 1.53)
Myoclonic status	0/1	0/2	0/3
Seizure-free (last visit)	?	1/2	2/3 (66.7%)

### **Epilepsy in patients with UBE3A mutations**

	Minassian et al., 1998	Moncla et al., 1999	Laan et al., 1999	Our series
No. of cases/M	2/0	14/8	8/6	10/6
Epilepsy	2/2	11/14 (78.6%)	5/8 (62.5%)	8/10 (80%)
Typical EEG	2/2	14/14	6/8 (75%)	10/10
Age (last follow- up)	10-18 yrs	5-36 yrs (17,57 ± 9,80)	4-53 yrs (23.5 ± 14.84)	3-32 yrs (16.42 ± 10.40)
Age at seizure onset	18 yrs (case A64)	6 mos-20 yrs (5.14 ± 5.43)	?	1-4 (2.5 ± 1.07)
Myoclonic status	0/2	?	?	3/8 (37.5%)
Seizure-free (last follow-up)	1/2 (50%)	7/11 (63.6%)	2/5 (40%)	4/8 (50%)

### Seizure types

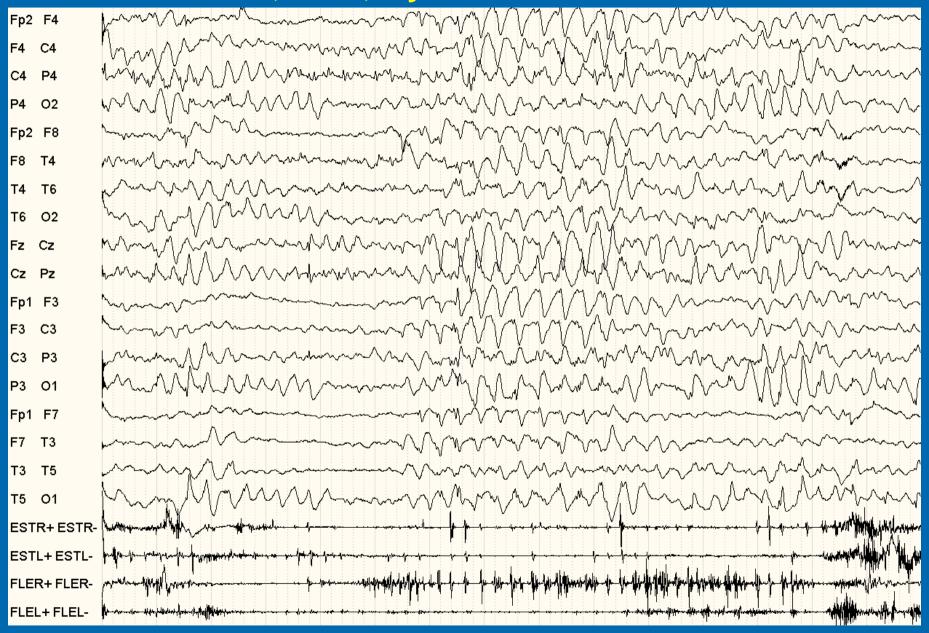


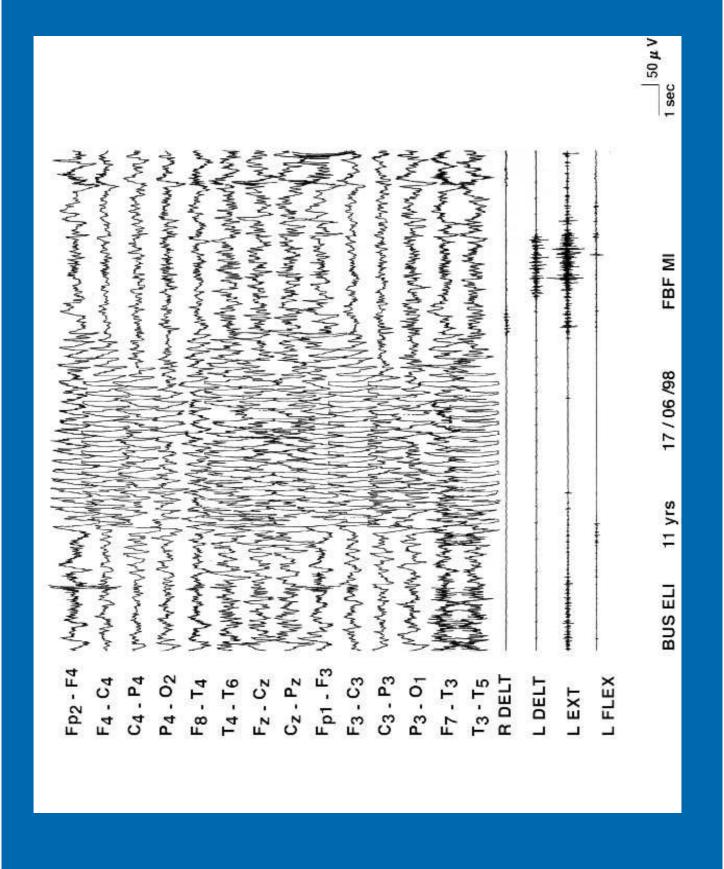
### Frequency of the seizures\*

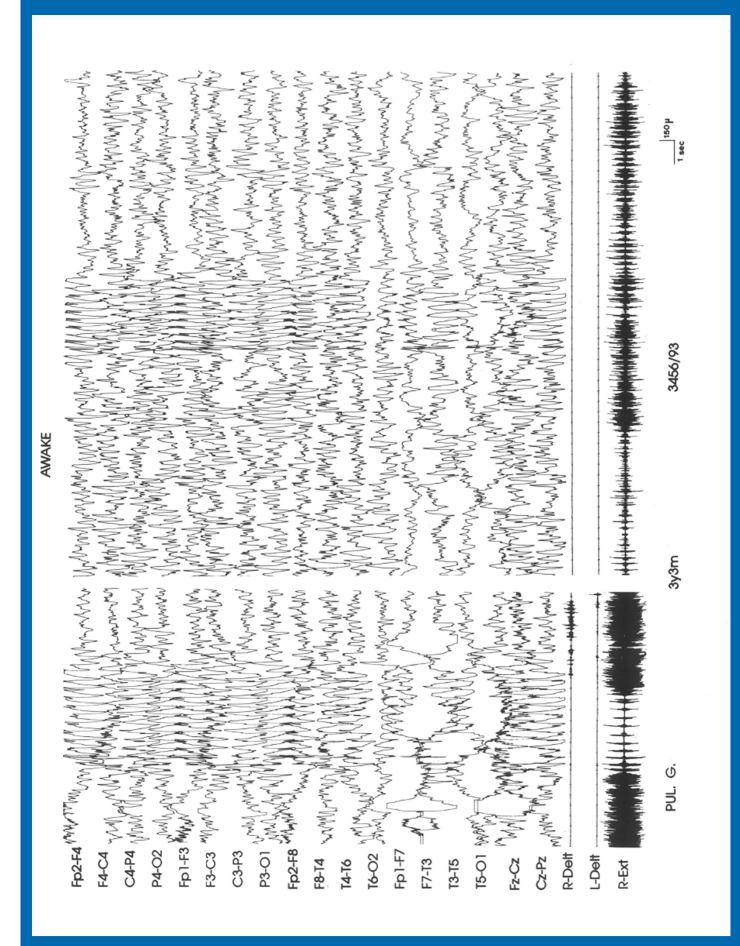
>1/day	1
>1/week	2
>1/month	1
>1/year	5
sporadic	4

<sup>\*</sup> subjects presenting seizures at the last visit (n=13)

### S.A., male, 5 yrs old - Wakefulness







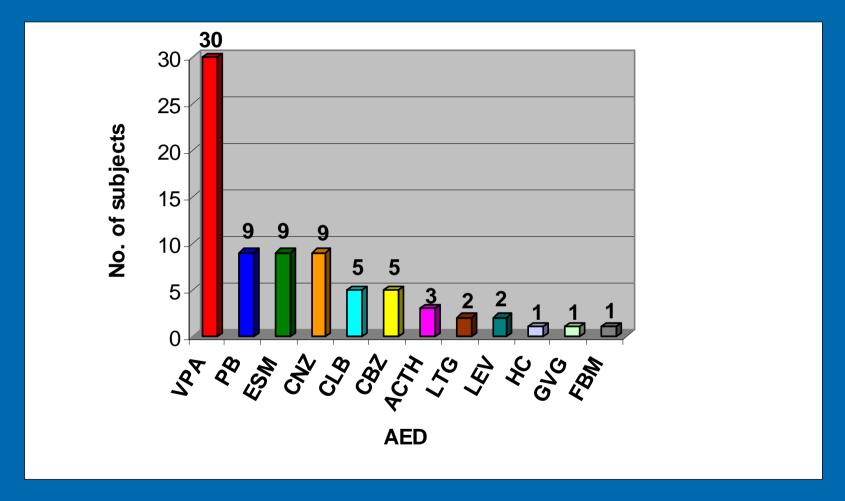
### **EEG**

- in 30/34 subjects (88.2%) EEG disclosed multifocal posterior SWs
- > in 3/34 patients (8.82%) multifocal frontal paroxysmal abnormalities (SWs) were present
- → in 6/34 patients (17.65%), multifocal frontal and posterior SWs were found
- in 3 cases focal (central or temporal) SWs were present
- in 18/28 sleep recording spindles and K complexes were recognizable

### Clinical and EEG pattern: DD

- > fetal and neonatal anoxic injury (cerebral palsy)
- newborn continuous partial epilepsy: initial neurological picture is normal; the jerks are more rhythmic; a severe progressive intellectual deterioration quickly appears
- pepileptic encephalopathy: cognitive deterioration; drug-resistant seizures; presence of tonic and atonic seizures
- Wolf-Hirschhorn syndrome (4p-): slow BA & 2-3 Hz high-voltage slow-wave bursts biparietally, mainly elicited by eye closure; SW complexes, and high-voltage bifrontal slow-wave bursts
- trisomy 12p syndrome: diffuse SW complexes; myoclonic-like absences; "myoclonic status" never reported

### **AEDS\***



\*only 3/34 patients (# 2,14, 17) never took AEDS; 2 of them had no seizures 1 patient (#28) discontinued AEDs 1 patient without seizures (#3) was treated with AEDs

### Number of AEDS at the last visit

