e-Table-2: The proportion of patients that met each of the latest criteria for congenital Rett Variant (Neul *et al.*, 2010) The spectrum of features is similar in females and males.

|  |  |
| --- | --- |
|   | Number of *FOXG1 positive cases* |
|   | Female (n = 23) |   | Male (n=22) |   | Total |
|   | ≤ 5 y (n = 10) | > 5 y (n = 13) | All |   | ≤ 5 y (n = 10) | > 5 y (n = 12) | All |   |   |
| Necessary criteria |   |   |   |   |   |   |   |   |   |
| A period of regression (+/-followed by recovery) | 2/10 (20%) | 4/13 (30,8%) | 6/23 (26,1%) |   | 4/10 (40%) | 0/11 (0%) | 4/21 (22,7%) |   | 10/44 (22,7%) |
| Main criteria |   |   |   |   |   |   |   |   |   |
| Partial or complete loss of acquired hand use  | 3/10 (30%) | 1/13 (7,7%) | 4/23 (17,4%) |   | 0/10 (0%) | 0/11 (0%) | 0/21 (0%) |   | 4/44 (9,1%) |
| Partial or complete loss of acquired spoken language  | 0/10 (0%) | 0/13 (0%) | 0/23 (0%) |   | 0/10 (0%) | 0/12 (0%) | 0/22 (0%) |   | 0/45 (0%) |
| Gait abnormalities (impaired / dyspraxic) or absence of ability | 10/10 (100%) | 13/13 (100%) | 23/23 (100%) |   | 10/10 (100%) | 12/12 (100%) | 22/22 (100%) |   | 45/45 (100%) |
| Stereotypic hand movements | 10/10 (100%) | 12/13 (92,3%) | 22/23 (100%) |   | 4/10 (40%) | 8/10 (80%) | 12/20 (60%) |   | 34/43 (79,1%) |
| Supportive criteria |   |   |   |   |   |   |   |   |   |
| Breathing disturbances when awake  | 0/6 (0%) | 1/11 (9,1%) | 1/17 (5,9%) |   | 3/9 (33,3%) | 0/7 (0%) | 3/16 (18,7%) |   | 4/33 (12,1%) |
| Bruxism when awake | 1/5 (20%) | 5/6 (83,3%) | 6/11 (54,5%) |   | 6/9 (66,7%)  | 4/9 (44,4%) | 10/18 (55,6%) |   | 16/29 (55,2%) |
| Impaired sleep pattern | 7/10 (70%) | 5/11 (45,4%) | 12/21 (57,1%) |   | 7/10 (70%) | 8/11 (72,7%) | 15/21 (71,4%) |   | 27/42 (64,3%) |
| Abnormal muscle tone including truncal hypotonia and/or spasticity | 9/9 (100%) | 13/13 (100%) | 23/23 (100%) |   | 10/10 (100%) | 10/12 (83,3%) | 20/22 (90,9%) |   | 42/44 (95,4%) |
| Peripheral vasomotor disturbances | 1/5 (20%) | 4/6 (66,7%) | 5/11 (45,5%) |   | 0/7 (0%) | 1/5 (20%) | 1/12 (8,3%) |   | 6/23 (26,1%) |
| Scoliosis/kyphosis | 2/10 (20%) | 4/12 (33,3%) | 6/22 (27,3%) |   | 1/10 (11,1%) | 3/11 (27,3%)  | 4/21 (19%) |   | 10/43 (23,3%) |
| Growth retardation (most recent weight +/- height below -2SD) | 2/10 (20%) | 6/11 (54,5%) | 8/21 (38,1%) |   | 3/8 (37,5%) | 3/10 (30%) | 6/18 (33,3%) |   | 14/39 (35,9%) |
| Small cold hands or feet | 1/6 (16,7%) | 2/4 (50%) | 3/10 (30%) |   | 1/7 (14,3%) | 1/5 (20%) | 2/12 (16,7%) |   | 5/22 (22,7%) |
| Inappropriate laughing / screaming spells | 2/9 (22,2%) | 9/11 (81,8%) | 11/20 (55%) |   | 8/10 (80%) | 5/10 (50%) | 13/20 (65%) |   | 24/40 (60%) |
| Diminished response to pain | NE | NE | NE |  | NE | NE | NE |  | NE |
| Intense eye communication "eye pointing" | 1/10 (10%) | 3/13 (23,8%) | 4/23 (17?4%) |   | 2/9 (22,2%) | 2/12 (16,7%) | 4/21 (19%) |   | 8/44 (18,2%) |
| Congenital Rett variant specific criteria |   |   |   |   |   |   |   |   |   |
| Grossly abnormal inital development | 10/10 (100%) | 13/13 (100%) | 23/23 (100%) |   | 10/10 (100%) | 12/12 (100%) | 22/22 (100%) |   | 45/45 (100%) |
| Severe postnatal microcephaly (below -4 SD) | 8/10 (80%) | 3/12 (25%) | 11/22 (50%) |   | 6/9 (66,7%) | 9/11 (81,8%) | 15/20 (75%) |   | 26/42 (61,9%) |
| Regression in the first 5 months | 1/10 (10%) | 3/13 (23,1%) | 4/23 (17,4%) |   | 2/6 (33,3%) | 0/11 (0%) | 2/17 (11,8%) |   | 6/40 (15%) |
| Lack of intense Rett gaze (poor eye contact but present) | 10/10 (100%) | 13/13 (100%) | 23/23 (100%) |   | 10/10 (100%) | 12/12 (100%) | 22/22 (100%) |   | 45/45 (100%) |
| Small cold hands or feet | 1/6 (16,7%) | 2/4 (50%) | 3/10 (30%) |   | 1/7 (14,2%) | 0/5 (0%) | 1/12 (8,3%) |   | 4/22 (18,2%) |
| Peripheral vasomotor disturbances | 1/5 (20%) | 4/6 (66,7%) | 5/11 (45,5%) |   | 0/7 (0%) | 1/5 (20%) | 1/12 (8,3%) |   | 6/23 (26,1%) |
| Breathing disturbances when awake  | 0/6 (0%) | 1/11 (9,1%) | 1/17 (58,8%) |   | 2/9 (22,2%) | 0/7 (0%) | 2/16 (2,5%) |   | 3/33 (9,1%) |
| Tongue stereotypies | 3/7 (42,8%) | 5/9 (55,5%) | 8/16 (50%) |   | 4/8 (50%) | 1/9 (11,1%) | 5/17 (29,4%) |   | 13/33 (39,4%) |
| Jerky movements of the limb | 9/10 (90%) | 10/13 (76,9%) | 19/23 (82,6%) |   | 9/10 (90%) | 11/12  | 10/22 (45,4%) |   | 29/45 (64,4%) |
| Meets criteria for Congenital Rett Variant |   |   |   |   |   |   |   |   |   |
| Necessary criteria | 2/10 (20%) | 3/13 (23,1%) | 5/23 (21,7%) |   | 4/10 (40%) | 0/11 (0%) | 4/21 (19%) |   | 9/44 (20,4%) |
| Two of the four main criteria | 10/10 (100%) | 13/13 (100%) | 23/23 (100%) |   | 3/10 (30%) | 8/10 (80%) | 11/20 (55%) |   | 34/43 (79,1%) |
| 5 Of the 11 supportive criteria | 0/4 (33,3%)  | 7/7 (100%) | 7/11 (63,6%) |   | 3/5 (60%) | 3/6 (50%) | 6/11 (54,5%) |   | 13/22 (59,1%) |
| All criteria | 0/9 (0%) | 2/12 (16,7%) | 2/21 (9,5%) |   | 1/10 (10%) | 0/11 (0%) | 1/21 (4,76%) |   | 3/42 (7,1%) |

Abbreviations NE : not evaluated ; SD standard deviation.