

Videogame-based coordinative training can improve advanced, multisystemic early-onset ataxia

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Dear Sirs,

Treatment options are rare in neurodegenerative childhood-onset ataxias, especially if presenting in advanced disease stages and with multisystemic disease load. Moreover, wheelchair-bound children and young adults with ataxia are commonly excluded from current drug treatment trials [1, 2], thus leaving them without prospects of access to novel treatments. Using a rater-blinded intraindividual control design, we here provide first proof-of-principle evidence that videogame-based coordinative training might serve as an effective treatment even for advanced, multisystemic degenerative ataxia.

A 10-year-old boy suffering from genetically confirmed Ataxia Telangiectasia (compound heterozygous *ATM*

p.Glu2596Aspfs*4 and p.Asp1625_Ala2626delinsGluPro) since 3 years of age and wheelchair-bound with only residual standing and walking capacities since 7 years of age (clinical details, Supplement 1) was recruited for a sequentially structured 12-week coordinative training program based on specifically selected, commercially available Nintendo Wii[®] games (for details, see Fig. 1a). The subject was examined four times: 5 weeks before the intervention (E1), immediately before the first training phase (E2), after the first home training phase (E3) and after the second home training phase (E4). Delta E1–E2 was taken as an intraindividual control period to control for changes associated with a monthly intravenous application of 750 mg methylprednisolone per day for 3 days which had been initiated by the patient's local physicians > 8 months before the study. Dosis and interval were kept constant before and throughout the study. The outcome measures were: (1) clinical degree of clinical ataxia severity, rated by means of videotaped Scale for the Assessment and Rating of Ataxia (SARA) [3] scores presented in a random order to an ataxia specialist (J.W.) blinded to the number of the specific examination (E1–E4); (2) quantitative movement analysis of balance capacities in sitting (methodological details, [4, 5] and Supplement 3); and (3) achievements in patient self-selected individually important goals with respect to standing and sitting, assessed by the goal attainment score (GAS) [6] (Supplement 4). This study has been approved by the appropriate ethics committee and has been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments.

The SARA score of 26.5/40 points, indicating an advanced disease stage, remained unchanged before training (E1–E2), thus demonstrating no major effect of corticosteroids or substantial fluctuations in the natural history

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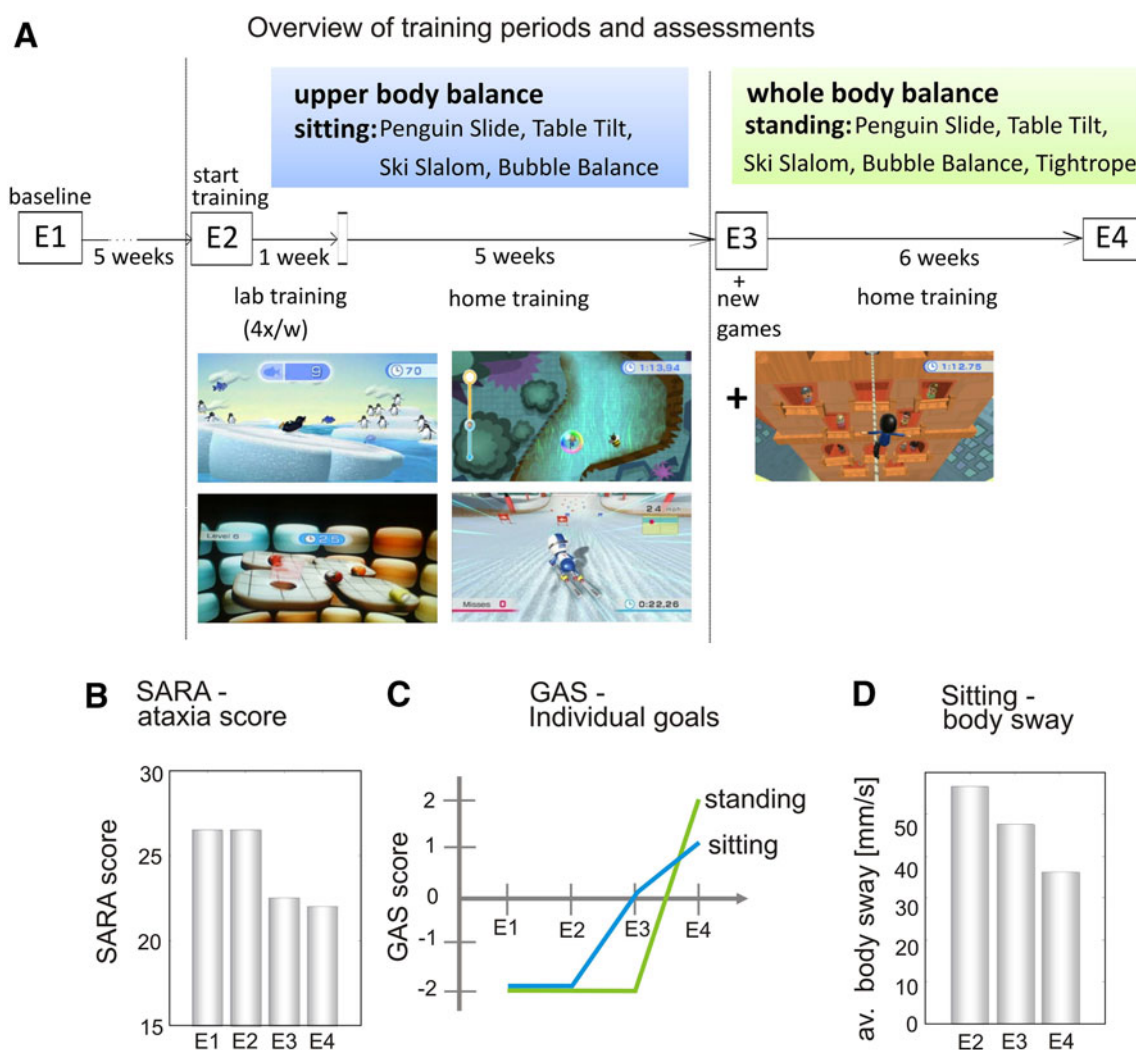


Fig. 1 Design of the training study and training results. **a** Design of the training study. The program was sequentially structured: (1) 1-week lab-training supervised by a physiotherapist; (2) 5-week home-training with continuation of the exercises at home without physiotherapist; (3) two update-training sessions within 2 days, supervised by a physiotherapist; (4) 6-week home-training with continuation of the exercises at home without physiotherapist. The update training sessions allowed to increase the training complexity by introducing more complex videogames, depending on the learning progress of the subject. Commercially available Nintendo Wii® games were selected to train arm and upper-body coordination in the first training phase (E2 until E3): “penguin slide”, “table tilt”, “bubble balance”, and “ski slalom”, all played while sitting. To train

standing and whole-body balance in the second training phase (E3 until E4), the same games, plus the game “tightrope walk”, were played while standing (for details, Supplement 5). **b** Scale for the Rating and Assessment of Ataxia (SARA) throughout the study course. Minimal score: 0 points; maximal score: 40 points. **c** Goal attainment score (GAS) for standing and sitting. Scores range from -2 to $+2$ (-2 regression from current level, -1 current level of performance, 0 expected level of performance, $+1$ greater than expected outcome, $+2$ much greater than expected outcome). **d** Average body sway during sitting, assessed by quantitative movement analysis before (E2), during (E3), and after (E4) the intervention. Since the subject was able to sit only with assistance at E1, sitting could not be reliably recorded at E1

of the disease. Throughout the training (E2–E4), it dropped by 4.4 points (Fig. 1b). This rater-blinded improvement is equivalent to gaining back functional performance of 3 or more years of disease progression (assuming a 1.4 point SARA increase per year, as shown for Friedreich’s ataxia [7]). SARA improvements were most pronounced in posture and gait (for illustration, see Supplement 2). Correspondingly, subjective achievement ratings show marked

balance improvements in sitting and stance (Fig. 1c, Supplement 4), and quantitative movement analysis in sitting (Fig. 1d, Supplement 3; stance not reliably recordable due to need of assistance).

This case study used a rater-blinded intraindividual control design to control for any observer biases and changes related to individual disease progression or medication. It shows that children with ataxia might benefit

from videogame-based coordinative training with effects that translate into daily living—even if in advanced disease stages and if suffering from multisystemic neurodegenerative disease (including oculomotor and cognitive deficits). This presents an important extension of a recent study from children with mild-to-moderate ataxia affecting mainly the spinocerebellar pathways [5]. It illustrates that neurorehabilitative learning is possible despite advanced neurodegeneration. This is important, as most treatment trials currently focus only on early disease stages and even deny access for children who are already wheelchair based (e.g., [2]). This inexpensive novel training method might hold many advantages for children with advanced movement disorders, as it can be easily performed at home and is highly enjoyable.

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