**Title**: Spatial Abilities in Aging Adults with Down Syndrome: Normative Aging and Implications for Dementia

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**Introduction**: People with Down syndrome (DS) have a higher likelihood of developing Alzheimer’s Disease (AD). Previous research has shown that deficits in spatial abilities could serve as predictors of early stages of AD (Mandal et al., 2012). Here, we aimed to examine the normative development of spatial abilities in individuals with DS and whether different spatial tasks could differentiate the different stages of dementia (i.e., cognitively stable (CS), mild cognitive impairment (MCI), and dementia).

**Method**: This study used the dataset from the ABC-DS project, a large-scale longitudinal study that tracks cognitive and health outcomes in individuals with DS across the lifespan (Handen et al., 2020). The sample consisted of 376 participants with DS (204 males; 359 Caucasian; 362 non-Hispanic), with a mean age of 45.34 years old (SD = 9.86; range = 25 to 81). An expert committee classified the participants into four groups: 259 CS (no MCI/dementia), 53 with MCI, 45 with dementia, and 19 as undetermined. Relevant to the current study, we focused on two spatial construction tasks (Block design, Down Syndrome Mental Status Exam (DSMSE -Visuospatial)), a spatial-motor integration task (the Beery Buktenica Developmental Test of Visual Motor Integration or VMI), and a spatial memory task (DSMSE-Memory). The total scores of DSMSE were used to indicate general cognitive ability (Krinsky-McHale et al., 2020).

**Results**: After accounting for general cognitive ability and intellectual impairment level, hierarchical regressions showed that age was a significant predictor for VMI and DSMSE-memory but not for Block Design or DSMSE-spatial. See Table 1. After excluding the “undetermined” group, one-way ANOVAs showed significant differences between groups on all spatial tasks. We then evaluated the discriminative sensitivities of four spatial tasks in distinguishing between CS, MCI, and dementia groups using ROC (Receiver Operating Characteristic) analyses. DSMSE-memory had the highest predictive power for differentiating between groups, especially between the CS and dementia groups (AUC = .921). The combined models had the highest AUC, yet Delong’s test found that the combined models did not differ from the individual models of DSMSE-memory. See Table 2.

**Discussion:** Spatial abilities in adults with DS showed different sensitivities to age. More specifically, spatial-motor integration and spatial memory are more susceptible to age-related declines but not for visuospatial construction. Spatial memory showed the best discriminative ability to differentiate between groups suggesting that it could serve as a valuable tool for detecting early markers of cognitive decline in adults with DS. Future research should continue to refine spatial assessments as diagnostic tools and explore the efficacy of interventions aimed at preserving and enhancing cognitive function, including spatial cognition, for aging adults with DS.

**Table 1. Hierarchical Regression Results**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| DV | IV |  | β | t | Sig | R2 | ∆R2 |
| Block Design | Step 1 |   |   |   |   |   |   |
|   | DSMSE - Total | .459 | 7.05 | **<.001** |   |   |
|   | ID level | -.134 | -2.07 | **.040** | **.301\*\*** |   |
|   | Step 2 |   |   |   |   |  |   |
|   | DSMSE - Total | .422 | 6.23 | **<.001** |  |   |
|   | ID level | -.162 | -2.43 | **.016** |  |   |
|   | Age | -.100 | -1.82 | .070 | **.310\*\*\*** | .009 (p=.07) |
| VMI | Step 1 |   |   |   |   |  |   |
|   | DSMSE - Total | .427 | 6.44 | **<.001** |  |   |
|   | ID level | -.142 | -2.14 | **.033** | **.274\*\*\*** |   |
|   | Step 2 |   |   |   |  |  |   |
|   | DSMSE - Total | .372 | 5.43 | **<.001** |  |   |
|   | ID level | -.183 | -2.73 | **.007** |  |   |
|   | Age | -.152 | -2.73 | **.007** | **.295\*\*\*** | **.021\*\*****(p=.007)** |
| DSMSE-spatial | Step 1 |   |   |   |   |  |   |
|   | DSMSE - Total | .486 | 7.49 | **<.001** |  |   |
|   | ID level | -.102 | -1.57 | .118 | **.305\*\*** |   |
|   | Step 2 |   |   |   |   |  |   |
|   | DSMSE - Total | .457 | 6.75 | **<.001** |  |   |
|   | ID level | -.124 | -1.86 | .064 |  |   |
|   | Age | -.081 | -1.47 | .144 | **.311\*\*\*** | .006 (p=.144) |
| DSMSE-memory | Step 1 |   |   |   |   |  |   |
|   | DSMSE - Total | .498 | 9.17 | **<.001** | **.249\*\*** |   |
|   | Step 2 |   |   |   |  |  |   |
|   | DSMSE - Total | .429 | 8.35 | **<.001** |  |   |
|   | Age | -.339 | -6.60 | **<.001** | **.359\*\*\*** | **.110\*\*\* (p<.001)** |

**Note:** \*\*\* p<.001, \*\*p<.01. Significant results were also in bold. DV: dependent variable, IV: independent variable.

**Table 2**. AUC values

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|   | Test Variable(s) | AUC | SE | p | 95% CI |
| Comparison | Lower | Upper |
| CS vs. MCI |   |   |   |   |   |   |
|   | Block Design | .700 | .045 | .000 | .611 | .788 |
|   | VMI | .674 | .041 | .000 | .593 | .754 |
|   | DSMSE - Visuospatial | .686 | .039 | .000 | .609 | .763 |
|   | DSMSE - Memory | .725 | .041 | .000 | .645 | .804 |
|   | All 4 variables | .779 | .031 | .000 | .718 | .840 |
| CS vs. Dementia |   |   |   |   |   |   |
|   | Block design | .877 | .028 | .000 | .823 | .931 |
|   | VMI | .774 | .046 | .000 | .685 | .864 |
|   | DSMSE - visuospatial | .801 | .042 | .000 | .718 | .884 |
|   | DSMSE - memory | .921 | .020 | .000 | .881 | .960 |
|   | All 4 variables | .937 | .017 | .000 | .905 | .970 |
| MCI vs. Dementia |   |   |   |   |   |   |
|   | Block design | .683 | .055 | .001 | .575 | .791 |
|   | VMI | .664 | .060 | .006 | .547 | .781 |
|   | DSMSE - Spatial | .687 | .059 | .001 | .572 | .802 |
|   | DSMSE - memory | .777 | .048 | .000 | .684 | .871 |
|   | All 4 variables | .804 | .045 | .000 | .715 | .893 |

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