Impact of cognitive reserve on dance intervention-induced changes in brain plasticity

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Abstract

Dance is a complex sensorimotor activity with positive effects on physical fitness, cognition, and brain plasticity in the aging population. We explored whether individual levels of cognitive reserve (CR) proxied by education moderate dance intervention (DI)-induced plasticity assessed by resting-state functional connectivity (rs-FC) changes of the sensorimotor network (SMN), and between the dorsal attention network (DAN) and anterior default mode network (aDMN). Our cohort consisted of 99 subjects, randomly assigned to either a DI group who underwent a 6-month intervention ($n = 49$, $M_{age} = 69.02 \pm 5.40$) or a control group ($n = 50$, $M_{age} = 69.37 \pm 6.10$). Moderation analyses revealed that CR moderated DI-induced increases of the SMN rs-FC with significant changes observed in participants with ≥ 13 years of education ($b = .05$, $t(64) = 3.20$, $p < .001$). Only DI alone was a significant predictor of the DAN-aDMN crosstalk change ($b = .06$, $t(64) = 2.16$, $p = .03$). The rs-FC increases in the SMN were correlated with an improved physical fitness measure, and changes in the DAN-aDMN connectivity were linked to better performance on a cognitive task. Consistent with the passive CR hypothesis, we observed that CR correlated only with baseline behavioral scores, not their change.

Introduction

Dance is a complex sensorimotor activity that involves learning new motor skills, utilizes attentional action observation and imitation, and integrates sensory, motor, and cognitive demands[1] that bestow rehabilitating effects even on an aging brain. Considerable experimental research on dance intervention (DI) in the elderly has shown compelling benefits in postural and gait parameters[2], physical fitness[3], and cognition in the memory[4,5], attention[2,6], and psychosocial domains[7]. Overall, DI-induced behavioral benefits are key in preserving mobility and independence in older age[8] and the importance of studying them stems particularly from the low efficacy of current pharmacological treatment for dementia patients[9].

Our previous research of an optimized, structured six-month-long dance intervention (DI) on non-demented seniors demonstrated its positive effects in comparison with “life activities as usual” (LAU) on the performance of the 8-Foot Up-and-Go (8UG) and the 30-Second Chair Stand (30CS) tests[10] which target dynamic balance, agility, lower body strength, and physical endurance[8]; and of the Five Point Test (FPT)[11,12], which assesses figural fluency, i.e. the ability of executive functions to provide information about divergent reasoning, divided attention, planning, and mental flexibility[13]. Interestingly, despite the fact that figural fluency is known to decline in the healthy elderly and particularly in patients with Alzheimer’s disease (AD)[14], the observed improvements were independent of hippocampal volumes[11]. This finding indicates an individual capacity to recruit additional neural resources in order to meet the demands of the intervention. To test this hypothesis, the current work aims at studying neural changes associated with the described behavioral improvements in terms of neural compensation. This accords well with Lövdén and colleagues, who postulated that any acquisition of new skills (dancing, in our case) requires changes in neuronal connections provided by the brain’s capacity for plasticity termed as a cognitive reserve (CR)[15]. CR is usually proxied by lifetime exposure to cognitively enriching activities[16,17] with "years of education" being the most common proxy of CR[18]. The CR bridges the disjunction between brain pathology load and preserved cognition by compensating for decreased neural efficiency, particularly in elderly or diseased individuals[19]. This is achieved by various mechanisms, among which the increased engagement and connectivity of large-scale brain networks plays an important role[17,20]. Several authors attempted to examine CR-related changes at the level of resting-state brain networks with inconclusive results[21]. Others showed that the level of CR has an impact on the association between the magnitude of resting-state connectivity and cognitive outcomes. For example, lower anti-correlation between an anterior (frontal) part of the default mode network (aDMN) and the dorsal attention network (DAN) was linked with decreased memory performance in those amnestic mild cognitive impairment (aMCI) patients who had low CR (proxied by education and IQ), but not in those with high CR levels[22]. In other words, higher levels of CR alleviated the impact of disrupted inter-network crosstalk on cognition.

In the current study, we aimed to explore the extent to which the individual level of CR moderates the intervention-induced ability to recruit behaviorally-relevant neural resources as assessed by resting-state fMRI. We were specifically interested in the resting-state functional connectivity (rs-FC) changes of the sensorimotor network (SMN) and in the inter-network connectivity changes between the DAN and the aDMN, with the ventromedial prefrontal cortex (vmPFC) as a representative region. The rationale behind the first network of interest was the fact that the SMN connectivity increases in response to motor training[23–25]. The SMN is a set of highly interconnected somatosensory, primary motor, and premotor regions that coordinate action and operate in a hierarchical fashion to translate visual and rule-based information into appropriate motor responses[26]. Regarding the DAN-aDMN, theta burst stimulation applied over the left superior parietal lobule (i.e. the major node of the DAN) in our previous non-pharmacological study successfully induced the deactivation of the aDMN node in the anterior cingulate cortex encompassed in the vmPFC and decreased reaction times on the Stroop task performance[27]. The DAN consists particularly of the bilateral superior parietal lobules/ intraparietal sulci and the frontal eye fields, and since it contributes to the formation of task rules and goals by top-down orienting, it is engaged especially during externally directed tasks[28]. Conversely, the DMN is a set of highly interconnected brain regions active when the mind is not engaged in specific behavioral tasks and suppressed (deactivated) during goal-directed behavior with focused attention[29]. The anterior part of the DMN is particularly connected to the parietal regions of the DAN, and it has been associated with attention and memory functions[30]. It has been well documented that the magnitude of the rs-FC between the task-positive DAN and the task-negative DMN plays a central regulating role within functional networks underlying cognition[31]. Patterns of the DAN-DMN connectivity reflect cognitive control efficiency and working memory[29] as well as episodic memory performance[22,32].

Taken together, there is a sufficient evidence that CR buffers the impact of normal or pathological aging on cognition. Individuals with high CR are more capable of drawing brain plasticity changes on the scale of rs-FC[21], which may compensate for the brain pathology load by alleviating its decremental impact on cognition[33]. The abovementioned studies have motivated our aim to study the moderating effects of CR in the context of intervention-induced benefits. More specifically, we directly probe the effect of DI on rs-FC changes at different levels of education as a proxy of CR.

Results

Baseline measures and their changes: comparisons of the groups. No significant baseline differences were found between the DI (n = 49) and the LAU (n = 50) groups in sex ($X^2(1) = 2.77$; p = .10), demographic data, screening of general cognition (MoCA), behavioral tests of interest, or in the connectivity of networks of interest. Note that 68 participants (DI: 36, LAU: 32) had complete fMRI data. All relevant baseline measurements and their changes are depicted in Table 1. As reported in our previous works[10,11], changes in the FTP, 8-Foot Up-and-Go, and 30-Second Chair Stand test scores significantly differed between the DI and the LAU groups. Similarly, the change in the rs-FC of DAN-aDMN significantly differed between both groups. For baseline and follow-up comparisons of cognitive tests that were not included in the present text, see Kropacova and colleagues[11]; no significant baseline differences were found.

Variables	Baseline variables				Change of variables (time$_2$-time$_1$)			
	DI	LAU	*t(df)*	*p*	DI	LAU	*t(df)*	*p*
	M ± SD	M ± SD			M ± SD	M ± SD		
Age	69.10 ± 5.43	68.37 ± 6.10	-.63(97)	.53	-	-	-	-
Education	14.53 ± 2.58	14.80 ± 3.10	.47(97)	.64	-	-	-	-
MoCA	26.92 ± 2.85	26.06 ± 2.71	-1.53(97)	.13	-.20 ± 2.42	.66 ± 2.37	1.80(97)	.075
FPT	28.39 ± 8.36	31.12 ± 9.48	1.52(97)	.13	.54 ± .92	-.02 ± 1.09	-2.81(97)	.006
8UG	5.08 ± 1.21	5.23 ± 1.28	.60(96)	.55	-.31 ± .76	.31 ± 1.22	2.98(93)	.004
30CS	15.85 ± 3.51	16.43 ± 4.53	.70(95)	.49	1.58 ± 2.62	.31 ± 2.36	-2.46(91)	.02
SMN	.54 ± .10	.58 ± .18	1.17(48.25)	.25	.04 ± .16	-.01 ± .15	-1.27(66)	.21
DAN-aDMN	.06 ± .08	.08 ± .12	1.03(53.51)	.31	.02 ± .10	-.03 ± .11	-2.23(66)	.03

Table 1. Baseline and follow-up demographic comparison of two experimental groups based on the independent-samples t-tests. *DI* – Dance-intervention group; *LAU* – Life-as-usual group; *Age* and *Education* in years; *MoCA* – Montreal Cognitive Assessment score; *FPT* – Five-Point Test score; *8UG* - 8-Foot Up-and-Go score in seconds; *30SC* – 30-Second Chair Stand test score; *SMN* – internetwork connectivity of the sensorimotor network; *DAN-aDMN* – connectivity between the dorsal attention network and the anterior default mode network; *M* – mean; *SD* – standard deviation.

Correlation analyses. Baseline fitness scores were mutually correlated (r = − .57, p < .001), as well as the FPT with the 8-Foot Up-and-Go task (r = − .32, p = .001) and with the 30-Second Chair Stand test (r = .29, p = .002), pointing to approximately 10.2 and 8.4% shared variance, respectively. The baseline rs-FC of the SMN and of the DAN-aDMN were not correlated with any of the baseline behavioral tests of interest. Finally, the Pearson’s correlations of improvement in the 8-Foot Up-and-Go task with increased connectivity within the SMN [r = − .21, p = .046), 95% CI (-.52, .04)], and improvement in the FPT with the rs-FC change in DAN-aDMN [r = .19, p = .056, 95%CI (-.05, .43)] did not reach the expected Šidák-Dunn value of $\alpha = .017$.

Moreover, education was positively related to all baseline behavioral scores: FPT (r = .38, p < .001), the 8-Foot Up-and-Go task (r = − .18, p = .04) and the 30-Second Chair Stand test (r = .27, p = .004), but not to their changes. Consistently with the moderation model (see below), education correlated only with rs-FC change within the SMN in the DI group (r = .41, p = .007) but not with its baseline; it did not correlate with either the baseline rs-FC between DAN-aDMN nor with the between-network rs-FC change.

Moderation analyses. The moderation analysis of rs-FC change within the SMN revealed that CR moderates the effect of DI on the network change, i.e. the effect of dance depended on years of education. No main effect was significant in this model and only the interaction effect was observed. Upon closer inspection of the Johnson-Neyman zone of significance, we observed a significant positive effect in higher values of CR (≥ 13 years of education; operationalized as W = .458; 44.12% of cases), which diminished in moderate values of CR. Conversely, as CR decreased (≤ 10 years of education; W = -4.885; 4.41% of cases) the relationship between DI and rs-FC change was significantly negative (Fig. 1).

As for the DAN-aDMN between-network rs-FC, the moderation analysis revealed that changes were dependent on the main effect of program; the effect of CR or the interaction were not significant. Despite that, Johnson-Neyman zones of significance yielded the most significant effect of the program at the moderate levels of CR (13 to 15 years of education; W = − .907 to 1.353; 39.71−60.29 percentile). The regression coefficients and t values that emerged from the moderation analyses of rs-FC changes are presented in Table 2.

Model terms	B [95% CI]	SE B (HC4)	t	p
SMN change				
Constant	-.003 [-.057, .050]	.027	-.124	.902
Cognitive reserve (centered)	-.017 [-.036, .002]	.009	-1.746	.086
Program	.050 [-.023, .123]	.037	1.365	.177
Moderator CR*program	.046 [.017, .074]	.014	3.199	.002
DAN-aDMN change				
Constant	-.034 [-.076, .008]	.021	-1.618	.111
Cognitive reserve (centered)	-.001 [-.017, .015]	.008	-.177	.860
Program	.058 [.004, .111]	.027	2.160	.034
Moderator CR*program	.008 [-.014, .029]	.011	.734	.466

Table 2. Linear model of predictors of change in SMN connectivity ($R^2 = .163$; $F(3,64) = 5.135$; $p = .003$) and DAN-aDMN connectivity ($R^2 = .081$; $F(3,64) = 1.574$; $p = .204$). Results are unstandardized beta coefficients with 95% confidence intervals from moderation models estimating the association of program, CR, and their interaction with

rs-FC change. Note: only continuous variables that contributed to the outcomes were centered. Cribari-Neto model was used for standard error of variance and F-statistics. Variable program coded as *LAU*: 0, *DI*: 1; SMN – inter-network rs-FC of the sensorimotor network; *DAN-aDMN* – between-network rs-FC of dorsal attention network and anterior part of the default mode network.

Discussion

Dance is a joyful complex activity combining physical exercise with cognitive, social, musical, and artistic stimulation[34]. The benefits of dance intervention stem from the recruitment of higher-order cognitive functions that require enhanced engagement and coordination of large-scale brain networks[35]. This study followed up on our previous findings showing that DI elicits distinct motor[10] and cognitive improvements[11]; it focused on the moderating effects of CR proxied by education on the DI-induced rs-FC changes involving the large-scale brain networks, namely the SMN and the DAN-aDMN.

We observed that the rs-FC increase of DAN-aDMN was dependent on the DI, while the changes in the SMN intra-network connectivity depended on the interaction between the DI and education. In other words, the follow-up changes within the SMN network were not significant across the whole DI group but only in those with higher CR. This result is discussed in more detail in the context of CR moderating effects in the text below.

All the baseline behavioral (fitness and cognitive) scores as well as their follow-up improvements were mutually correlated, sharing approximately 10% of their variance. This variance can represent a shared component of psychomotor speed, which declines throughout the lifespan[36].

Regarding our neuroimaging results, previous literature showed that dance practice may modify brain plasticity as evaluated by structural MRI[12,37], but little is known about the rs-FC changes induced by the DI. By comparing professional and naïve dancers, Burzynska and colleagues[34] demonstrated differences between both groups in the engagement of the general motor learning network, including major nodes of the SMN, basal ganglia structures, and frontoparietal regions. The current study employed rs-fMRI and for the first time explored the CR moderation of brain plasticity changes resulting from the DI. Our major finding supported the significant CR moderation of the DI effect on the rs-FC changes within the SMN. Specifically, the observed increase of the SMN rs-FC was dependent on ≥ 13 years of education (which equals the minimum of secondary education with graduation in the Czech schooling system). This effect dissolved in moderate levels and significantly reversed in low levels of CR (≤ 10 years of education). Note that only 4.41% of the cases had such a low education level, and thus this latter result cannot be further interpreted. The observed DI-induced increase of rs-FC of the SMN is clinically relevant as it was associated with improved performance in dynamic balance and mobility, known to decline with aging[8]. The SMN is particularly engaged in motor learning and execution of specific motor actions[38]; although the SMN has not been assessed in the context of DI, studies on aerobic exercise interventions have consistently reported a reactive increase of rs-FC of the SMN in healthy[24] and diseased subjects[39], as well as significant differences in its structural connectivity among professional ballet dancers in comparison to a control group[40]. The relation between education level and motor network involvement may seem peculiar; nevertheless, associations between motor aspects and education levels have been demonstrated. For instance, in Parkinson's disease patients (i.e. the typical patient group with a movement disorder) the CR (proxied by education) was inversely correlated with motor symptom severity despite greater reductions in dopamine levels[41,42].

In contrast, the moderation model of the DAN-aDMN rs-FC changes revealed that the DI alone, without CR contribution, is a significant predictor of its change. Although the results yielded the most prominent effect for those with secondary education, the interaction effect was not significant, and therefore, this latter finding has to be taken with caution. The DMN-DAN connectivity plays an important role in cognitive control and working memory[27,29], which is significantly altered with aging[43]. Anthony and Lin[44] speculate that individual hub seeds of the DMN, including the anterior cingulate region, underlie the core hub of *neural reserve* in the context of CR, while the DAN regions are rather related to *neural compensations* (i.e. engaged in brain maintenance to compensate for brain pathology). Therefore, our results are in line with the notion that by increasing the DAN-aDMN crosstalk, dancing may facilitate neuroplasticity and the preservation of CR[45]. A prospective 21-year study demonstrated that regular participation in dancing was the only physical activity among the 11 studied (e.g. bicycling, playing tennis or swimming) that was associated with a lower risk of dementia in an elderly cohort, presumably by increasing plasticity and CR[46].

Interestingly, while higher levels of CR were related to better baseline behavioral scores, they were not correlated with their follow-up changes. Even though ours is the first study to observe such discrepancies resulting from an intervention, many longitudinal observational studies, and particularly those conducted on samples with a degenerative brain disease, found that CR (proxied by education, occupation, or premorbid IQ) was related to baseline behavioral outcomes, but not to their changes[47,48]. For instance, higher education among PD patients predicted lower incidence of high Hoehn-Yahr stage, better cognitive and motor baseline scores as estimated by MMSE and gait speed with UPDRS-III respectively, but not their annual progression of 6 years[49]. This phenomenon has been dubbed a passive reserve hypothesis and highlights the CR contribution to better cognitive and motor performance scores resulting from the persistence of differences that appear at younger ages, rather than from ongoing changes (e.g. lifestyle or pathology) that influence differential rates of cognitive decline[49].

There are limitations to our study. We used a static proxy of CR which may not be reflective of the dynamic nature of the CR and its pathology-induced depletion[50]. Estimating dynamic CR using a latent or residual CR index[51,52] in future research might deepen our understanding of its reactive nature. Besides, educational attainment is contaminated with socioeconomic factors, such as income, access to health care, gender, and healthy lifestyle habits. Finally, adaptive testing is a more sensitive approach to training or evaluation in uncovering post-intervention effects.

In conclusion, the protective effects of cognitive reserve in nondemented older adults have been suggested by several lines of research. We showed that an intensive six-month DI can induce clinically-relevant changes in brain plasticity, physical fitness, and cognition, and importantly, that some of the brain plasticity changes depend on education, a proxy of CR, suggesting that higher capacity for plasticity applies to better intervention outcomes. Our study also demonstrated that the DAN-aDMN rs-FC, a potential neural representation of CR, can be modulated by DI. Future studies should employ multimodal comprehensive programs to benefit people across different CR levels[36]. Despite our clinically-relevant results, it is unknown whether short-term engagement in any set of activities is sufficient to elicit changes that last several months or even years after the intervention completion. Therefore, long-term behavioral outcomes of such interventions should be examined and long-lasting moderation effects of CR should be tested.

Materials And Methods

Sample. A total of 99 community-dwelling, non-demented elderly subjects completed the main study and were described in detail previously[10–12]. All subjects were over 60 years of age without any medical, neurological, or psychiatric disorders that may have an impact on cognition (such as major depression, drug and/or alcohol abuse), or would interfere with DI or with MRI scanning. The absence of dementia was assessed by a screening of cognitive decline (MoCA), the Functional Activities Questionnaire, and a detailed cognitive battery (see Table 1S in the Supplementary Material). Subjects were randomized to a dance intervention group (DI) (N = 49) or a control (LAU) group (N = 50). For detailed information about the enrolment and randomization process, see Kropacova and colleagues[11]. Informed consent was obtained from each subject. The study was approved by the ethics committee of Masaryk University and in accordance with the ethics code and regultions. Each subject underwent a neurological examination, detailed neuropsychological evaluation, MRI, and physical fitness examination prior to the program and six months after the program completed.

Dance intervention. The DI program was designed and supervised by specialists from the Faculty of Sports Studies, Masaryk University, Brno, Czech Republic. The whole study lasted for three years with the yearly rotation of a group of 20 subjects. Each intervention took six months and included three training units (each of 60 minutes) per week. The DI program was supervised and conducted at a medium physical load intensity which was monitored each session using the Borg Rating of Perceived Exertion (RPE) scale, a user-friendly numerical scale that evaluates an individual's subjective effort, physical exertion, and fatigue during exercise on a 15-point scale[53]. The DI sessions included folk, country, African, Greek, and tango dancing. The choreographies were divided into smaller blocks that were gradually taught in individual lessons and modified and developed over time into the final choreography. Only subjects who completed at least 60% of the DI program were included in the final cohort[11]. The real average completion of the DI program was 78.1%.

Physical fitness examination. The effect of the DI was evaluated using two tests from the functional fitness assessment[8]. The 8-Foot Up-and-Go Test evaluates agility and dynamic balance. It measures the time (in seconds) required to get up from a seated position, walk an eight-foot distance, return to the chair, and sit down. Lower values indicate better performance. The 30-Second Chair Stand test evaluates lower body strength and physical endurance by measuring the number of repetitions of full stands from a chair in 30 seconds. Higher values indicate better performance. Scores on both tests improved in the DI group as compared to LAU group [10].

Neuropsychological examination. Global cognition (MoCA), activities of daily living, and five cognitive domains were evaluated by complex neuropsychological testing (see Table 1S in the Supplementary Material). The five domains included memory, attention, executive, visuospatial, and language domain. In the current study, we focus on the Five-Point Test (FPT) performance which significantly improved in the DI group as compared to LAU group [11].

MRI examination. All subjects were scanned using the 3T Siemens Prisma MRI scanner (Siemens Corp., Erlangen, Germany) employing various sequences including the T1 anatomical and diffusion tensor imaging sequences[10,12]. For the purpose of this study, we used resting-state fMRI data, employing gradient-echo echo-planar imaging sequence (200 scans, 34 transversal slices, slice thickness = 3.5 mm, TR = 1990 ms, TE = 35 ms, FA = 70°, FOV = 192 mm, matrix size 64×64).

fMRI data processing. Resting-state fMRI data were preprocessed using the SPM 12 toolbox and Matlab 2014b. Preprocessing started with realignment and unwarping. Next, cardiac and respiratory signals were regressed out using RETROICOR[54]. Then, normalization into standard anatomical space (MNI) and spatial smoothing with 5 mm FWHM was performed. The level of motion was thoroughly checked in terms of frame-wise displacement (FD)[55]. No FD was higher than 3 mm and scans that displayed FD > 0.75 mm were scrubbed[55]. No more than 2.5 % of subject scans were removed. Moreover, the six movement regressors (obtained during realignment and unwarping), FD, and extracted signals from white matter and cerebrospinal fluid were regressed out of the data in the subsequent analysis. Representative seeds (spheres with 6 mm radius) of large-scale functional brain networks of interest (SMN, DAN) and a vmPFC seed representing the aDMN were chosen based on a literature review[56]. MNI coordinates for each seed and network are listed in the Supplementary Material (Table 2S). Mean seed signals were extracted and a correlation matrix was calculated for each subject. Pearson's correlation coefficients were converted to z values using Fisher's r-to-z transformation. The connectivity within the SMN and between the DAN-aDMN were calculated as the average of z values within the network seed pairs[57].

Analyses of the CR effects on DI-induced changes in rs-FC. Demographics between the two study groups were compared using t-tests for continuous variables and chi-square tests for categorical variables. The CR was represented by years of education[18]; the program variable had two dimensions – dance intervention (DI) or control life as usual (LAU); changes in the outcome variables of interest were computed as timepoint_2 (a follow-up visit after 6 months) - timepoint_1 (baseline). In the moderation analyses, the effect of CR (moderator variable) was tested on the relationship between the program (independent variable) and change in functional outcomes of interest. The first set of moderations was performed on 68 subjects who had complete fMRI data (36 DI and 32 LAU) to assess whether and to what degree the relationship between DI and rs-FC changes within the SMN and between the DAN-aDMN depend on CR levels. Moderation was selected because it enables inferring the effect of CR and program and their interaction (CR*program) and also modeling the effects of different levels of the CR moderator (on + 1SD, 0SD, and − 1SD CR). This approach simplifies the interpretation of results when such effects are present based on the zone of significance without the necessity of subsequent sets of single main effect tests. All data were normally distributed.

As discussed briefly, in addition to the moderation analyses, we also conducted one-tailed Pearson correlations between baseline and follow-up change of behavioral and rs-FC outcomes, and with education independently of the intervention. This was to test the association of behavioral outcomes and the rs-FC changes of interest, as well as their relationship with years of education.

All statistical analyses were performed using IBM SPSS Statistics 27. For moderation analyses, we used the PROCESS macro for SPSS v 3.4. Finally, the Šidák-Dunn correction was set for each dataset independently in the following manner: $1 - (1 - \alpha)$ ^ ½ = .025 for the two moderation models; $1 - (1 - \alpha)$ ^ $^1/_6$ = .009 for the behavioral correlations (between three behavioral tests and their correlation with CR), and $1 - (1 - \alpha)$ ^ $^1/_3$ = .017 for the three correlations between rs-FC changes and behavioral tests.

Declarations

Data Availability

The datasets analysed during the current study are available from the corresponding author on reasonable request.

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Author contributions

Study conception and design: K.M., I.R., P.V., A.S., R.G; data collection: K.M., A.SM., S.K., Z.B., P.K., P.V., A.S., R.G; analysis and interpretation of results: K.M., P.K., J.T.; draft manuscript preparation: K.M.; All authors reviewed the results and approved the final version of the manuscript.

Additional information

None of the authors has a financial/non-financial competing interest to declare.

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Figures

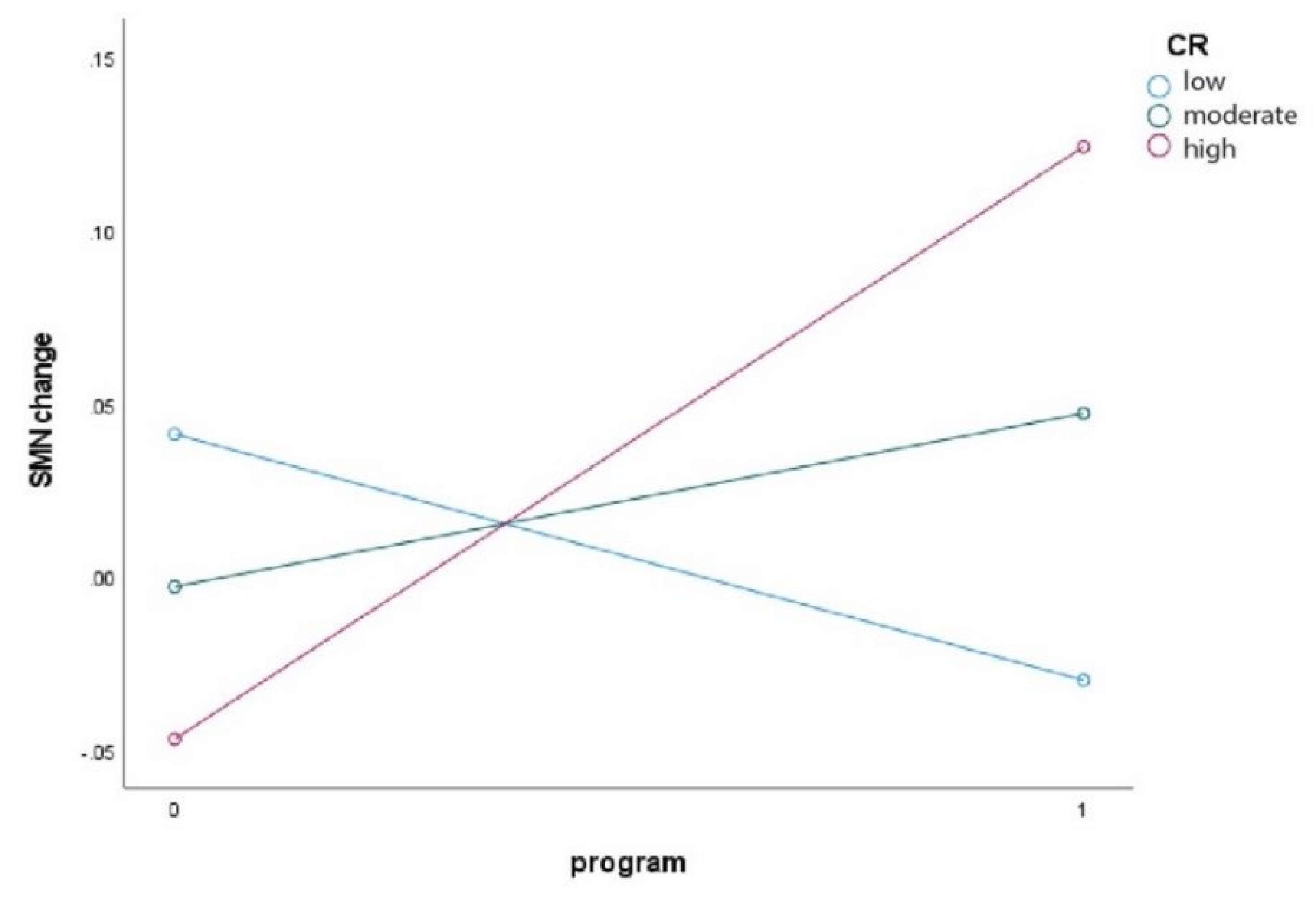

Figure 1

Slope analysis according to z-scores. In participants with relatively high CR (red), there was a significant positive relationship between the program and change in the rs-FC within the SMN, b = .171, 95% CI [.080, .261], t = 3.767, $p < .001$. In participants with moderate (green) and low CR (blue), there is a non-significant relationship between the change and the program (b = .050, 95% CI [-.023, .123], t = 1.365, p = .177, and b = -.07, 95% CI [-.189, .047], t = -1.204, p = .233, respectively. Note: Variable program coded as LAU: 0, DI: 1. SMN – inter-network rs-FC of the sensorimotor network.

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