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**Mesenchymal Foxc1 non-autonomously controls cerebellar development through SDF1 $\alpha$ -CXCR4 maintenance of radial glial cells**

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Foxc1 mutations have been implicated in Dandy–Walker malformation (DWM), the most common human cerebellar malformation diagnosed by an enlarged posterior fossa and fourth ventricle, and cerebellar hypoplasia. Although loss of this transcription factor causes developmental cerebellar pathology, it is not expressed in the developing cerebellum. Rather it is widely expressed in embryonic mesoderm and mesenchyme including the developing posterior fossa beginning  $\sim$ e12.5 in mice.

We now demonstrate that loss of mesenchymal Foxc1 expression at e12.5 induces a rapid and devastating reduction in cerebellar ventricular zone radial glial proliferation and survival, and a concurrent dramatic increase in cerebellar neuronal differentiation as early as e13.5. Subsequent radial migration of remaining Purkinje cells is also disrupted, associated with a disordered radial glial morphology. Through a combination of *in vitro* proliferation and migration assays, we determine that SDF1 $\alpha$ , a direct downstream target of Foxc1, expressed in the head mesenchyme, acts as a cerebellar radial glial survival factor and mitogen, and also a chemoattractant for nascent Purkinje cells. We show that the SDF1 $\alpha$  receptor, Cxcr4, is specifically expressed in cerebellar radial glial cells. Ablation of Cxcr4 in cerebellar radial glial cells largely mimics the Foxc1 mutant cerebellar phenotype. Our data demonstrates that SDF1 $\alpha$ -Cxcr4 signaling is essential for radial glial survival and function. This is an earlier and more fundamental role for this important signaling pathway in cerebellar development than previously reported. Our DWM and Foxc1 data contributes to a growing body of evidence supporting a paradigm shift. The brain does not develop in isolation. Rather, the head mesenchyme exerts considerable influence on early embryonic brain development.

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## ISDN2014.0120

**Meranzin hydrate exhibits anti-depressive and prokinetic-like effects through regulation of the shared alpha2-adrenoceptor in the brain-gut axis of rats in the forced swimming test**

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**Background:** in recent years, the brain-gut axis theory has received increasing attention in studies of depression. However, most studies separately address potential antidepressant and prokinetic treatments. Investigations of drugs that could

potentially treat comorbid depression and gastrointestinal (GI) dysfunction via a common mechanism of action have not yet been performed in detail.

**Aim:** To and a common mechanism of action of our patented drug, meranzin hydrate (MH), in the antidepressant and prokinetic treatment.

**Methods:** The forced swimming test (FST) model of depression, plasma ghrelin measurement, and *in vivo* and *in vitro* measurements of GI motility were used.

**Results:** 1. Administration of MH (9 mg/kg) decreased the immobility time during the FST after acute treatment; this effect was inhibited by the alpha 2-adrenoceptor antagonist, yohimbine, but not by the alpha 1-adrenoceptor antagonist, prazosin. 2. After chronic treatment, the immobility time of rats during the FST was decreased significantly by MH (2.25 mg/kg). 3. MH (9 mg/kg) increased plasma ghrelin levels in rats subjected to the FST; this increase was enhanced by the ghrelin receptor agonist, GHRP-6. 4. MH (9 mg/kg) also promoted gastric emptying and intestinal transit in rats with or without FST. 5. *In vitro*, MH (10  $\mu$ M) increased jejunal contractions in rats subjected to the FST; this effect was inhibited by yohimbine. Furthermore, the inhibitory effect of yohimbine was partly reversed by the ghrelin receptor agonist, GHRP-6.

**Conclusion:** Our study revealed that MH from natural resources exhibits antidepressant and prokinetic-like effects through the regulation of the common mediator, the alpha 2-adrenoceptor.

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## ISDN2014.0121

**Creative thinking abilities among children and adults with dyslexia**

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This study investigated the figural and verbal creative abilities of learning disabled (LD), children and adults. The creative abilities of two sub-groups of LD children, verbal/auditory and visual/spatial were compared. Also, the association between handedness and creativity was assessed.

There were 28 LD and 29 non-LD (non-learning disabled) children from 5 years 11 months to 11 years 1 month. The two groups were matched on the parameters of sex, age, Block Design and handedness. Also, 12 dyslexic and 12 non-dyslexic adults matched on sex, age and handedness participated in the study.

The results indicated no significant differences between LD and non-LD children in any measures of creativity. The creativity of both groups was associated with age. Although the verbal/auditory sub-group did not score higher than non-LD children, their figural creativity was associated with left-handedness. The visual/spatial sub-group performed less well than non-LDs on the figural creativity task. Dyslexic adults surpassed non-dyslexic adults on almost all measures of creativity. Their enhanced performance was not associated with their handedness.

These results are discussed in the context of the enhanced right hemisphere theory. In addition, it is suggested that creative abilities of dyslexics may develop with age. Also, subtypes of dyslexia should be considered when researching creativity in relation to learning disability.

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