Further evidence that infantile autism is a chronic psychosis distinguished by a Deficient Delayed Response Function affecting the connections between Hippocampus and Singulum in its center, the SMA and the inhibitory Purkinje cells in cerebellum

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Abstract
Older literature on infantile autism accompanied by mental retardation, focussed on epilepsy, cerebral palsy and microcephaly. Multiple adversity was needed to delay growth sufficiently to pruning of connection between Hippocampus and Singulum in its centre, SMA and inhibitory cells in Cerebellum in the synaptogenesis in infancy. Temporary macrocephaly was observed. Today, macrocephaly dominates the discussion. One single adversity, deficient “brain food”, seemingly retards growth sufficiently to cause excess pruning with absent activity in inhibitory Purkinje cells in Cerebellum, the SMA and A DEFICIENT, LACKING DELAYED RESPONSE FUNCTION. The brain needs time to
adapt, but the Delayed Response Task is lost. Microcephaly predominates at puberty. We wanted to understand cerebellar reactions more fully.

**Keywords**
The Delayed Response Task, adaptive events, synaptogenesis in infancy.

McGuire et al. (2000), employing a within-subject design, used functional magnetic resonance imaging to compare brain activity in patients when they were or were not experiencing auditory hallucinations but were engaged in inner speech. Activity patterns resembled those observed during periods of absent activity in the supplementary motor area (SMA) and in the cerebellum during hallucinations. Infantile autism (Saugstad, 2008), a chronic psychosis attributable to a second regressive event in infancy, is due to excessive synaptic pruning, which leads to absent activity in the SMA, the centre of the medial frontal lobe system that connects the hippocampus to the singulum. What particular symptoms are to be expected if the cerebellum is also pruned, leading to absent activity in the Purkinje cells?

The regressive event in infancy, affecting 40–70% of neuronal elements, starts in the posterior cortex (Kern, 2003). The risk of prefrontal pruning appears to be low, which is supported by statistics from Norway in the 1990s, when infantile autism was diagnosed in fewer than 5 per 10,000 births. Any adverse event in pregnancy or infancy (infection, bleeding, a genetic disorder) delays the rate of brain maturation. A number of mentally retarded children with infantile autism were studied – epilepsy and cerebral palsy were common findings, as was microcephaly, reflecting that multiple adverse events are needed to delay maturation sufficiently to result in pruning of the SMA and infantile autism: **chronic psychosis**: inability to plan conscious acts, to predict, plan according to storage of information (memory); an absent – defective delayed response function.

The situation prevailing today is quite different. A marked rise in the prevalence of infantile autism in Europe and the USA has been accompanied by a change in the clinical picture. Mental retardation, cerebral palsy and epilepsy in connection with infantile autism are discussed little, if at all. However, the prevalence of acute macrocephaly in infantile autism is reported to be rising. Acute macrocephaly usually persists until around 3–4 years of age, with head circumference being normal or slightly below normal by puberty. How is a temporary macrocephaly explained as a consequence of concomitant pruning of the Purkinje cells (Fiez and Raichle, 1997; Thompson et al., 1997)? Does the macrocephaly develop before the brain has adapted to the fact that the important inhibitory Purkinje cells are not functioning optimally? What do we know about the regressive events in the cerebellum? The Purkinje cells are supplied **proximally** by dendrites, with a multiplicity of climbing fibres connecting with each cell, and **distally** by parallel fibres with a one-to-one relation. Clearly, regressive events in infancy secure a one-to-one relation proximally with climbing fibres, thus optimizing their inhibitory function. This must be central to second regressive events in the cerebellum (Cesa and Strata, 2009; Hashimoto et al., 2009). Absent activity in the inhibitory Purkinje cells most likely explains a temporary macrocephaly because it would result in unusual excitability because the main inhibitors, the Purkinje cells, are dysfunctional. The brain needs
time to find a new balance; thus, we observe the development of macrocephaly, which disappears after a few years. At puberty head circumference is close to normal, or slightly reduced. However, children with infantile autism and macrocephaly used to be the most severely affected, suffering from various additional dysfunctions – cognitive as well as motor – as well as the characteristic absent delayed response function.

Furthermore, evidence (Thompson et al., 1997) suggests that the cerebellum is involved in the memory storage process in associative learning. It might even be pivotal in this central defect in autism. Pruning of the cerebellum together with the central SMA in the medial frontal lobe system fully explains the symptoms of autism. With these fundamental defects as regards our social brain, those affected develop a multiplicity of coping strategies and excessive use of vision, with those affected trying in vain to remember things despite their lacking a delayed response function and displaying anxiety towards any change in their environment. There has been no discussion of any possible influence of a deviation in development in infancy related to the second regressive event. The importance of these regressive events, such as synaptogenesis at around 6–7 months, was nicely demonstrated in van der Welt and van der Meer’s (2009) recent publication. They described how a 5-month-old infant used a large area of the brain in responding to an unexpected simple task, whereas at the age of 10–11 months only the particular localized brain area was involved, reflecting the effect of synaptic pruning, of which the authors appear unaware. It is remarkable that nobody has discussed the regressive events in infancy or at puberty, or their great variation in relation to the rate of growth and maturation, in the hunt for the cause of infantile autism. After all, these important events have been known for over 20 years. More importantly, they explain many unexpected findings in childhood as related to an excessively prolonged pruning, underlining the known advantage of early, fast maturation as we know it from birth weights.

Let us return to the rise in infantile autism in the USA, where currently 1 in 100 neonates or fewer are at risk of this diagnosis. Also, diagnoses of the disorders in Europe are increasing, despite no rise in any known risk factor. Remarkably good-looking individuals with infantile autism are pictured in the newspapers, with no mention of mental retardation or cerebral palsy. Apparently, they have not suffered multiple adversities. A single adverse event is seemingly capable of retarding growth and development to such a degree that both the SMA and the cerebellum are pruned, resulting in absent activity in accordance with both acute psychosis in an adult and chronic psychosis in infantile autism.

Let us consider the history of autism: both Kanner (1943) and Asperger (1944) considered their findings as psychological–psychiatric phenomena. Recall the refrigerator mother hypothesis proposed by Kanner: olfaction deficit at birth and cognitive dysfunction in childhood are due to a deficiency of brain food consumed by the mother during pregnancy, starving the olfactory bulb and hippocampus of the fetus. Similarly, a deficiency of brain food during infancy prolongs synaptogenesis sufficiently to result in absent activity in the SMA and cerebellum, thus causing a lack of or deficient delayed response function. Any link with a second regressive event at 6–7 months of age, an age when we usually master the delayed response function, is not mentioned. Tests for autism apply only to children aged 2–3 years, by which time the child with infantile autism has already suffered for 2 years. There is no mention of the absent delayed response function that distinguishes infantile autism: the inability to plan and predict
based on stored information (memory). We know from acute psychosis in adults that the cerebellum is silent, together with the SMA; similarly, in a prolonged second regressive event, both are pruned. In the past the majority of mentally retarded children with infantile autism were microcephalic, which reflects multiple adversities; the few with macrocephaly were among the more severely affected. Today only a small proportion of infants with autism are retarded, and macrocephaly is receiving increasing attention.

Let us return to the marked rise in infantile autism in the USA and Europe, despite no particular rise in any known adverse factor. The most important aspect of the striking rise in infantile autism and Asperger syndrome is that it is seemingly due to one single factor: insufficient ‘brain food’ during pregnancy and infancy is enough to retard brain growth and development to such a degree that the SMA, the centre of the medial frontal lobe network, is pruned. Admittedly, there are other disorders associated with ‘insufficient food for the brain’. Victims of sudden infant death syndrome have been reported to have birth weights, on average, some 200–300 g lower than those of their siblings and, more importantly, docosahexaenoic acid levels in the brainstem of the victims were significantly lower than in control infants. We ought also to remember that childhood epilepsy might be due to reduced brain-derived neurotrophic factor, delaying the transformation of excitatory $\gamma$-aminobutyric acid to inhibitory $\gamma$-aminobutyric acid, which is associated with a deficiency in food for the brain during pregnancy. An example of the result of undesirable behaviour in pregnancy is the recent striking rise in Asperger syndrome. In the presence of a continued inadequate diet, further delaying the rate of maturation to a pruning of the SMA in the second regressive event in infancy, Asperger syndrome might, in addition, develop into infantile autism.

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References


