

Neuropsychiatric aid in children born to patients with rheumatic diseases

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ABSTRACT

A chronic disease may have an adverse impact on patients' quality of life and on their relationship styles. If this occurs in a mother, the related emotional and physical distress can interfere with baby holding, impacting on the antenatal maternal-foetal attachment and on the upbringing and development of the baby. Ineffective holding leads to the persistence of a condition of "vulnerability to stress" and the possible development of psychosomatic problems in the offspring.

In this paper we present our experience and a review from the current literature on the psychological aspects of pregnancy and parenthood in women with rheumatic diseases (RD) and children's development.

To ameliorate family global quality of life, different experts (the rheumatologist, the obstetric, the neonatologist, the psychologist and the neuropsychiatric experts) should cooperate in teamwork to keep the patients' needs integrated. In particular, the neuropsychiatric intervention might support the patients and their partners throughout the experience of pregnancy and parenthood and prevent the occurrence of psychopathologic traits.

Introduction

Women with rheumatic diseases (RD) show a higher risk of spontaneous abortion, fetal loss, intrauterine growth restriction and preterm birth, when compared to the general population. In the last decades, the improvement in the diagnosis and the management of these diseases has resulted in a better care of the pregnant women affected by RD, with an increased possibility for them to have children. Meanwhile, the interest in the short- and long-term development of these children has

grown. It was observed that offspring of lupus mothers presented more learning, memory and behavioural problems when compared to children born to healthy mothers (1). Moreover, lupus mothers of children at risk for learning disabilities (LD) were positive for anti Ro/SS-A antibodies (2) and/or antiphospholipid antibodies (aPL) during pregnancy (3). Accordingly, a similar figure was found in children of women with primary antiphospholipid syndrome (APS) exposed to aPL during fetal life (4). The main hypothesis is that autoantibodies could react with the fetal cerebral tissue and, together with other well-known risk factors, such as prematurity, genetic and environmental factors, could contribute to the pathogenesis of LD.

Moreover, a strong association between autism spectrum disorders (ASD) and autoimmune disorders was observed. Children with autism show a higher prevalence of autoantibody and genes implicated in autoimmune disorders, when compared to the healthy subjects (5). A recent epidemiologic study has shown that a family history of autoimmune disorders is more common among children with ASD than in the offspring of parents with RD and healthy controls (6). Systemic lupus erythematosus (SLE) (7), adult rheumatoid arthritis (RA), type 1 diabetes (7, 8), hypothyroidism (7, 9), coeliac disease (8), rheumatic fever (9), psoriasis, and maternal asthma and allergy during the second trimester of pregnancy (6) have been described as associated with an elevated risk for ASD in the family members. In particular, as the number of family members with RD increases from 1 to 3, the risk of autism is greater, with an odds ratio that increases from 1.9 to 5.5, respectively (7). Some Authors (6) have suggested

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that autistic subjects might have experienced a prenatal antibody exposure due to maternal immune dysfunction. Together with other environmental and genetic factors, this altered foetal environment might be responsible for the ASD pathogenesis.

Meanwhile, the possible effect of maternal disease activity on the foetal brain development and on cognitive outcome has been studied (10, 11). Only a few papers are available on the psychological aspects of pregnancy and parenthood in women with RD and their children. In fact, a chronic disease may have *per se* an impact on patients' social life and on their relationships with the other family members, including the offspring (12), which can also influence children's development. It is well documented that a condition of stress during pregnancy or antenatal depression may play a role in the occurrence of preterm birth, lower birth weight, and, in newborns, higher vulnerability to stress (13, 14) together with less optimal neurobehavioural profiles (15). Throughout the children's lives, high *vulnerability to stress* will represent a latent, stable but dynamically modifyable condition that, when interacting with stress factors (chemical, environmental, psychological and physical), also including maternal disease, may challenge homeostasis and let a psychological or psychosomatic disorder occur.

Although psychological development can be considered the result of several interacting factors (temperamental, environmental, psychosocial, relational), we suggest that the relationship between children and parents affected by RD represents an important field of clinical investigation. In this paper, we present a review of the literature and data from our works in progress concerning the interaction between mothers with RD and their children. The neuropsychiatric intervention might prevent the occurrence of psychopathologic traits and its applicability will be discussed.

The impact of maternal rheumatic disease on pregnancy and on the first mother-baby relationship

It is reasonable to assume that different RD may influence the psychological

Table I. Case-control study conducted in a group of 23 RD pregnant women, compared to 19 healthy pregnant women. Cases' and controls' age and socio-economic status (calculated by the Hollingshead 4-factors index) were comparable. The subjects were asked to complete Cope, SF-36 and SAT-P for the evaluation of coping styles, quality of life and levels of satisfaction perception during their third trimester of pregnancy. We then carried out newborns clinical features at birth. Nine RD and 5 healthy women dropped out for difficulties in reaching the centre after delivery. Newborns' neurobehavioural outcome was carried out at one month of age, by the NBAS. In this table, we present the results that differentiate the two groups. The statistical tools used were Pearson χ^2 for categorical variables and Mann-Whitney U-Test for continuous variables.

I a. Differences in the areas of quality of life, perception of the daily life satisfaction, and coping skills in a group of pregnant women with RD and a group of healthy age-matched pregnant women.

	Pregnant women with RD (n=23) Median (IQR)	Healthy pregnant women (n=19) Median (IQR)	p-value
<i>Cope</i>			
Vent of emotions	12 (9.25–13.75)	9 (7.25–10.75)	0.013
Denial	4.5 (4.25–7)	4 (4–5)	0.048
Mental disengagement	8 (7–10)	7 (5.25–8.75)	0.034
<i>SF-36</i>			
Body pain	56.5 (41–93.5)	74 (62–92)	0.046
General health	59.5 (37–72)	82 (74.5–89.5)	0.000
<i>SAT-P</i>			
Work functioning	59 (43–80.3)	81.4 (68.2–89.5)	0.030

I b. Newborns' clinical features and neurobehavioural outcome at the age of one month, in the offspring of RD mothers when compared to those of healthy mothers.

	Offspring of mothers with RD (n=14) Median (IQR)	Offspring of healthy mothers (n=14) Median (IQR)	
Male (n. %)	8 (57.1%)	9 (64.3%)	n.s.
Gestational age (w.)	39.1 (36.6–40)	40 (40–40.25)	n.s.
Birth weight (gr.)	3136 (2625–3570)	3000 (2770–3507.5)	n.s.
<i>NBAS</i>			
Range of states scale	11.5 (7.75–15)	16 (10.75–17)	0.019
Reflex responses	6 (1.75–6.25)	1.5 (0.75–2.25)	0.002

IQR: interquartile range.
n.s.: not significant.

well being in different ways. In fact, a better quality of life, with lower levels of 'body pain', was described in pregnant women with RA (16) when compared to the healthy pregnant controls. On the other hand, a study in progress conducted by our group on a sample of 23 pregnant women with various autoimmune disorders (other than RA), matched with healthy controls, showed different results (17). A lower quality of life in the area of *body pain* and of the *general health* subsets (SF-36) (18), and a worst *work functioning* (SAT-P) (19) were referred (see Table Ia). This apparent discrepancy between RA and different RD may reflect the various

conditions of the patients during pregnancy: in fact, most women with RA experience a relief of pain as effect of pregnancy, also resulting in the reduction of drug intake. Therefore, since these patients usually suffer from high levels of pain, the physiologic gestational disturbances may be perceived as less painful, when compared to the healthy pregnant women. On the contrary, patients with other kinds of RD, such as SLE or APS, are usually advised to a strict control of their disease that can flare during pregnancy. Accordingly, Neri F. and colleagues (20) reported in women with SLE a state of anxiety for their health during pregnancy to-

Table II. Observational preliminary study on 11 women with RA. Inclusion criteria were that women had to suffer from RA since the period before pregnancy and had to have at least one offspring in school age (7 to 17 years). The 12 children enrolled, including 2 brothers (7 males and 5 females), had a mean age of 13.03 (SD=2.24), had a normal intelligence level (tested with WISC-R), and no neurological impairment. The parents were interviewed and also asked to complete the Child Behaviour Checklist (CBCL), a self-administered questionnaire that analyses behavioural and social offspring's characteristics to identify eventual risk of psychopathologies. In this table we present CBCL results, described as mean and SD, and as percentage of subjects at risk, in children born to mothers with RA.

	Children born to RA mothers (n=12) Mean (SD)
<i>Competence scale</i>	
Activity	3.9 (2)
Social	6 (1.5)
School	5.5 (0.3)
<i>Behaviour scale</i>	
Withdrawn	2.2 (1.8)
Somatic complaints	1.7 (2.3)
Anxious-depressed	3.5 (3.6)
Social problems	0.8 (1.1)
Thought problems	0.2 (0.4)
Attention problems	2.3 (2.5)
Delinquent behaviour	0.4 (0.7)
Aggressive behaviour	3.5 (3.8)
	Subjects at risk (%)
<i>Total competence scale</i>	8 (66.7%)
<i>Total behaviour scale</i>	0
<i>Internalising problems</i>	4 (33.3%)
<i>Externalising problems</i>	0

SD: Standard Deviation.

gether with the fear of transmitting the disease to the foetus in 18 (45%) out of the 40 patients interviewed.

It is well known that perceived stress and coping, which are two aspects strictly linked to mood balance, are more reliable predictors of positive or negative emotionality than disease severity (21). Coping strategies refer to the specific efforts, both behavioural and psychological, that people employ to tolerate or reduce stressful events; they are therefore correlated to the subjects' psychological well-being (22, 23). In our study, the 23 RD pregnant women used mainly coping strategies aimed at *denial*, *vent of emotions*, and *mental disengagement*, when compared to the healthy controls (see Table Ia). These *avoidant* coping strategies are considered not functional in a healthy subject's daily life and they are related to pregnancy-specific distress in healthy women (24, 25). In particular, coping by avoidance during pregnancy seems to significantly mediate the effects of uncertainty on psychological

well-being (26), especially in chronically ill pregnant women.

Afterwards, the presence of a chronic disease in the mother and the correlated emotional distress experienced can interfere with parenthood and baby holding, impacting on antenatal maternal-fetal attachment (27), the very first mother-baby relationship, and on the following upbringing and development of the baby (20). In a preliminary observation carried out by our group on a sample of 11 mothers with RA diagnosed before their pregnancies, 9 of them (75%) referred functional limitations which impaired child handling and care-taking in the first years of life. The most important difficulties of these patients consist in lifting, carrying, transporting and bathing their offspring (28). On the other hand, the fatigue, the functional disabilities and the chronic pain experienced by the mothers with RA may limit not only the caring of the offspring during childhood and adolescence (29, 30), but also they may support a hardly accepted feeling

of inadequateness and anxiety. Anxiety may, in turn, have a negative influence on mother's attunement to the baby's needs, on her and her child's relational styles and on the offspring's personality development.

Moreover, the persistence of avoidant coping strategies after delivery may lead to a dysfunctional maternal attitude towards the newborn. The consequent restraint of maternal thinking over the experiences shared between her and the baby may interfere on the handling of the physiological difficulties encountered during the upgrowing of the child. This reflective capacity usually allows the mother to find the better way to fit herself to the child's needs. When it fails, the newborn will go through the experience of an ineffective holding, leading to the persistence of a condition of *vulnerability to stress* and the possible development of psychosomatic problems.

Impact of maternal RD on the newborns' outcome and child psychological development

It is well-known that maternal distress and depression during pregnancy determine increased cortisol levels and decreased dopamine and serotonin levels. This hormonal environment may promote a premature delivery of low birth weight babies, as can be seen also in patients with RD under corticosteroids treatment (31). This imbalanced biochemical prenatal environment is related with less optimal neurobehavioural profiles in the neonates of distressed mothers (15).

Accordingly, in our previous study (32) the group of 14 children born to mothers with RD showed more problems than the healthy newborns (see Table Ib). In particular, 2 children were delivered very preterm (before 28 weeks of gestation) and 2 were small for gestational age.

At 1 month of corrected age, the newborns of RD mothers showed, at the Brazelton Neonatal Behavioural Assessment Scale (NBAS) (33), more difficulties at the *range of states scale* (which includes peak of excitement, rapidity of build-up, irritability, and lability of states) and more *reflex responses*

Table III. A possible scheme of a neuropsychiatric intervention from baby conception, through pregnancy, to child acquisition of the learning skills.

Timing	Aim of the neuropsychiatric clinical intervention	Neuropsychiatric tools
Before conception	Recognising subjects and couples at psychological risk	Counselling to the couple of possible future parents
During pregnancy	Accompaniment of the couple throughout the pregnancy	Longitudinal counselling to the couples. Mother: Test Cope for the evaluation of the coping styles
At birth	Focusing on parental experience of the delivery and of the first days together with the newborn Assessment of newborn's neurobehavioural development	Short interview to the parents Child: Brazelton NBAS
One month of life	Support to parenthood Assessment of maternal post-partum depression Assessment of newborn's neurobehavioural development	Counselling to the couple Mother: EPDS Child: Brazelton NBAS
Three months of life	Support to parenthood Assessment of maternal post-partum depression Assessment of newborn's neurobehavioural development	Counselling to the couple Mother: EPDS Child: neurobehavioural development observation scale
Six months of life	Support to parenthood Assessment of newborn's neurobehavioural development	Counselling to the couple Child: neurobehavioural development observation scale
Nine months of life	Support to parenthood Assessment of child's neurobehavioural development	Counselling to the couple Child: neurobehavioural development observation scale
One year	Pointing out the presence of psychosomatic disorders in the child, such as sleep problems, eating difficulties or dermatitis; support to parenthood Assessing child's psychomotor development	Counselling to the couple Child: Griffiths' Development Scales or Bayley Scale
Two years	Support to parenthood Pointing out the presence of behavioural or speech problems	Counselling to the couple Parents: CBCL 1½–5 years and Mac Arthur Communicative Development Inventory
Three years	Support to parenthood Assessing child's neurological, psychomotor and relational development	Counselling to the couple Child: Play observation, neurological evaluation and Griffiths' Development Scales or Bayley Scale
Five years	Pointing out the presence of a language disorder	Child: Screening for language disorders (performed by a speech therapist)
Eight years (for the offspring of SLE and APS mothers)	Pointing out the presence of a learning disorder	Child: Screening for learning disabilities (Italian protocol for the diagnosis of learning disorders: Battery of tests for the diagnosis of dyslexia and dysorthography of Sartori and Cornoldi; BDE and AC-MT for the diagnosis of dyscalculia)

than the healthy controls (see Table Ib). These problems might be determined by difficulties involving the first mother-baby relationship discussed above. Moreover, NBAS results were not significantly different when comparing the newborns with low gestational age and/or low birth weight and the newborns at term, with normal birth weight. When the maternal baby-caring is challenged by the presence of an invalidating chronic disease, such as RA, some other effects on children psychological growth may be observed. The baby may react to maternal failure by adapting himself to what the mother lacks and precociously develop an omni-

potent 'self-holding' function (34) that defends himself by the awareness of an anguishing dependence to the mother. According to this hypothesis, in our study 8 (66.7%) out of the 12 offspring (2 were brothers) were described by their mothers as 'hyper-mature', very early independent, behaving as an adult, very sensible and responsible, especially towards the mother's needs and worries. Patients appear to bear the weight of their disease with the offspring's help. In particular, the children's precocious autonomy seemed to work as a reassuring factor in respect of mothers' unthinkable feeling of inadequateness.

On the other hand, women could not "handle" enough the offspring's needs and this condition seemed to lead to the kids' inability to feel their own needs, but to recognise those of their mothers. The extreme consequence of this situation was represented by 2 daughters developing anorexia nervosa, the emblem of denial of personal and primary needs.

In our study, 4 out of the 12 school age children (33%), born to RA mothers, presented internalising problems at the CBCL behaviour problem scales, such as somatic complaints, depression and anxiety. Children showed a limited social life as if the development

of their relationship with the outside world could be conditioned by maternal disability. In fact, in 8 (66,7%) cases, the mothers described problems at the CBCL competence scale, which carries out children's socialising abilities, schoolmates integration, attention capacities, and free-time activities regarding hobbies or extra-familial and extra-school interests (see Table II). Low scores in the *activity* scales were also observed in children affected by chronic illness (35, 36).

Finally, in this case, the offspring of mothers with RA seemed to behave like the chronic sick children of the same age, as if the mothers' illnesses lasted upon them.

The role of the neuropsychiatric intervention

A brief scheme of the possible role of a neuropsychiatric intervention for mothers with RD, their partners and offspring during their first years of life together is illustrated in Table III. Different experts (rheumatologist, obstetric expert, neonatologist, psychologist and neuropsychiatrist) should effectively cooperate in teamwork to *handle* and keep integrated the patients' needs, as well as to ameliorate their global quality of life.

A step-by-step accompaniment of the woman with RD and her partner throughout the experience of becoming parents, should begin at the moment in which a couple expresses the desire to have a baby. In the case of patients with RD, the risk assessment usually performed before conception to women with a high-risk pregnancy could then involve not only biological but also the psychosocial and the psychological aspects that may lead to anxiety in the mothers and to a low neurobehavioural outcome in the newborns.

A counselling together with the rheumatologist and the obstetric expert could be the instrument to observe the specific needs of the couple, and also to recognise the patients at a major psychological risk. To assess patients' coping styles, the test Cope could be administered during the second trimester of pregnancy.

The neuropsychiatric expert could

then follow the evolution of the psychological aspects, related to the high risk pregnancy, through a longitudinal counselling to the couples singled out at a major psychological risk. Interventions aimed at promoting the use of active coping strategies by the mothers with RD and to increase the couples' awareness of each other's psychological concerns could reduce the risk of anxiety and postnatal distress in these patients (37).

After birth, the clinical follow up of newborns could also be integrated with the work of the neuropsychiatric expert who, supporting the mother and the father in their parental role, can introduce a specific attention to the child's neurobehavioural and psychological development. In order to assess at birth and at one month of life newborn's neurological and behavioural arrangement, the NBAS scale could be used. This scale also allows to show to the parents the various and complex skills of their baby, helping them to reduce anxieties and to get in touch with their *real* child. At 1 month, the assessment for maternal post-partum depression could be performed administering the Edinburgh Postnatal Depression Scale (EPDS) to the mother (38).

We suggest a 3-step counselling during the first year of life, since it represents a critical period of time for the development of a good relationship between the mother and her child. At 3 months, the EPDS scale administration should be repeated in order to study the evolution of possible depressive traits already observed, or to assess a later onset of a postpartum depression. At 3, 6 and 9 months, the evaluation of baby's development could be repeated using an observational scale of the neurobehavioural aspects.

The counselling to the parents should single out the child's neuro-developmental steps to reach postural control and hand manipulation skills, the child's general health, sleep, and eating behaviours, and the parental feelings of satisfaction and/or anxiety. This intervention should be aimed at supporting the parents to recognise their own and their child's competences.

Moreover, helping the child to reach

a more harmonious changing of states could promote a better development and a positive feedback to parental perception of their own competences, consequently reducing their anxieties and feeling of inadequateness.

In particular, the availability of a support to parenthood for RA mothers could promote a 'good-enough' relationship between them and their children during their first moments of life together, barring the development of a too precocious hyper-mature behaviour in their children.

At 12 months, the evaluation of infants' development should be aimed at considering child's general psychomotor achievements, such as locomotor, personal-social, hearing-speech, eye-hand coordination and the performance skills. The Griffiths' developmental scales number 1 (39) or the Bayley scales of infant and toddler development could be used for this purpose (40).

At 24 months, the counselling to the couple should be integrated with the assessment of children's behaviour and language development. In particular, the presence of emotional reactivity, anxious and/or depressive traits, eating and sleeping problems, and aggressive behaviour should be considered. The Child Behaviour Checklist 1½-5 years (CBCL 1½-5 years) (41) is a useful instrument, internationally used for this purpose. Moreover, the Mac Arthur Communicative Development Inventory (42), a parental report language assessment tool that uses a recognition format (parents check the words that their child produces), could be used for the first screening of speech development.

At 3 years of age, the psychomotor development should be assessed by repeating the Griffiths' developmental scales number 1 (or the Bayley scales of infant and toddler development). Particular attention should go to the language development. Cases recognised at risk for language delay should then undergo through a speech therapist evaluation and possible treatment. Early recognition and treatment of an abnormal speech development may reduce the severity of a language disorder and the risk for the future development of a specific LD. In fact, it is well

known that language delay and disorders often precede the development of a specific LD (43). A precocious therapy may also reduce the occurrence of relational and psychological problems, such as separation difficulties and depression, and socialising problems, such as maladjustment (44). In fact, these problems, together with other psychosocial risk factors (*i.e.* parental chronic disease and/or poor coping skills) are often associated to language and learning disorders, of which they also may play a co-causal role (45).

Moreover, a child playing observation and a neurological evaluation can be useful to integrate the information carried out through the counselling to the couple, as regards of the psychomotor and relational development.

Children recognised at risk for psychological or cognitive impairment might continue their longitudinal assistance under the care of the neuropsychiatric experts, who will adopt the specific intervention requested case by case. Because of the high prevalence of specific LD observed in the offspring of mothers with SLE or APS, this subgroup should undergo to a screening for the assessment of LD at 8 years of age. The instruments for the diagnosis of LD will be different accordingly to each Country guidelines. In Italy, the protocol for diagnosis of dyslexia and dysorthography is based on the Battery of test of Sartori and Cornoldi (46, 47, 48), while BDE test and AC-MT test (49, 50) are recommended to make a diagnosis of dyscalculia.

In conclusion, the neuropsychiatric intervention should first support the patients and their partners throughout the experience of pregnancy and of parenthood. In the long-term, the early identification of psychological difficulties and diagnosis of language and/or learning disorders in the offspring would be worthwhile, in order to help children to overcome their possible difficulties during the developmental years.

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